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=>  d his

     (FILE 'HOME' ENTERED AT 16:34:47 ON 20 JUN 2002)

     FILE 'REGISTRY' ENTERED AT 16:35:04 ON 20 JUN 2002
                 E HEPARIN/CN
L1               1 S E3
L2               1 S 81523-64-0
L3               1 S 50732-58-6
L4               1 S 81523-64-0
L5               1 S 81209-41-8
                 E HEPARIN/CN
L6               1 S SODIUM IMIDAZOLATE/CN
L7               1 S 5807-14-7
L8               1 S 81675-81-2
L9               1 S 81675-81-2
L10              1 S 98015-45-3
L11          67098 S N=3 AND (C AND H AND N)/ELS AND 3/ELC.SUB
L12           2997 S L11 NOT RSD/FA
L13            303 S L12 AND " GUANIDINE"
L14           5504 S L11 AND NR=2 AND NRS=1
L15             57 S "PYRIMIDO" AND L14
L16             23 S L15 AND "PYRIMIDINE"
L17            326 S L13 OR L16
L18              1 S 5807-14-7
L19            326 S L17 OR L18
L20            793 S P=1 AND N=4 AND (C AND H AND N AND P)/ELS AND 4/ELC.SUB
L21            114 S L20 NOT RSD/FA
L22            112 S L20 AND NR=1
L23              1 S SODIUM ACETATE/CN
L24              1 S HYDROGEN PEROXIDE/CN

     FILE 'HCAPLUS' ENTERED AT 17:06:26 ON 20 JUN 2002
L25          18203 S L1
L26             13 S L2-5
L27            162 S L6
L28           4638 S L7-10 OR L17 OR L21-22
L29          18213 S L25-26
L30            433 S L29(L)RCT/RL
L31           4798 S L27-28
L32           1497 S L31(L)RCT/RL
L33              1 S L30 AND L32
L34              1 S 2002:90113/AN
L35              0 S L33 NOT L34
L36          43501 S ?HEPARIN?
L37            255 S L36(S)QUAT?
L38            860 S L36 (5A)?ESTER?
L39             20 S L37 AND L38
L40           9113 S STRONG(3A)(BASE OR BASIC)
L41          64635 S ?GUANIDIN? OR ?PHOSPHAZEN? OR TRIAZA?
L42          27070 S PKA
L43              1 S L39 AND L40-42
L44              0 S L43 NOT L34
L45             13 S L37-38 AND L40-42
L46          16508 S DEPOLYMERI?
L47          78527 S DE(W)ESTERIF? OR SAPONIF?
L48              1 S L45 AND L46-47
L49              0 S L48 NOT L34
L50              6 S L30 AND L40-42
L51              1 S L50 AND L46-47
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heparin

claim 16

benzyl ester of heparin

strong bases

Cl 17

search for Cl 18

L20 - 22 search for Cl 20

L25 - 35 searching is based on Registry #'s

heparin

bases

heparin as a RCT

bases as a RCT

applicant's PCT

L36 - L113 searching is mostly based on Free text searching

L25 - L86 search is directed to the method of making

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L52         156 S L25-26 AND L40-42
L53         280 S L25-26 AND L46-47
L54           2 S L52 AND L53
L55           7 S L50 OR L54
L56           6 S L55 NOT L34
L57         379 S L36 AND L46
L58          43 S L36 AND L47
L59           1 S L57 AND L58
L60         366 S L36(L) L46
L61         230 S L36(5A) L46
L62          62 S L61 AND (DE(W)ESTER? OR REMOV? OR CLEAV? OR SAPONIF? OR BASE
L63          60 S L62 NOT L55
L64           1 S L63 AND ACETATE
L65      786430 S SODIUM OR (ALKALAI OR ALKALINE)(2A)(METAL)
L66           7 S L65 AND L63
L67       43921 S L25-26 OR L36
L68        1024 S L67(5A)L65
L69         117 S L68 AND  (DE(W)ESTER? OR REMOV? OR CLEAV? OR SAPONIF? OR BASE
L70           4 S L69 AND DEPOLYMER?
L71           2 S L70 NOT L55
L72           7 S L66 OR L71
L73           7 S L72 NOT L55
                E DEPOLYMER/CT
                E E10 +ALL/CT
L74       34532 S E3-8
L75         122 S L74(L)(L47 OR BASE OR BASIC OR PKA OR L28)
L76           0 S L75 AND (?HEPARIN? OR L25-26)
L77          54 S L74 AND (?HEPARIN? OR L25-26)
L78           5 S L77 AND (L47 OR BASE OR BASIC OR PKA OR L28 OR HYDROXIDE)
L79           4 S L78 NOT (L73 OR L55)
L80          22 S L68 AND (HYDROLYSIS OR HYDROLI?)
L81           1 S L80 AND L74
L82           0 S L81 NOT (L55 OR L73 OR L79)
L83          31 S L68 AND (HYDROL?)
L84          30 S L83 NOT  (L55 OR L73 OR L79)
L85           3 S L30 AND L84
L86           3 S L85 NOT  (L55 OR L73 OR L79)
L87        1263 S (L29 OR ?HEPARIN?)(S)L65
L88      609523 S KDA OR MW OR MOLECULAR WEIGHT OR KILODALTON OR KDA
L89         221 S L88 AND L87
L90         497 S ANTI-XA
L91         123 S ANTI-IIA
L92         311 S ?GLUCURONIC?(S)(END OR TERMIN?)
L93          30 S L89 AND L90
L94           7 S L89 AND L91
L95           1 S L89 AND L92
L96           7 S L93 AND L94
L97          51 S L89 AND XA
L98          17 S L89 AND IIA
L99          16 S L97 AND L98
L100         16 S L96 OR L99
L101          3 S L100 AND ?URON?
L102          2 S L101 NOT L34
L103         13 S L100 NOT L101
L104        694 S LMWH
L105         40 S L104(5A) L87
L106         35 S L105 NOT (L101 OR L55 OR L73 OR L79 OR L96)
L107          3 S L106 AND (?URON? OR ?SULPHAT? OR ?SULFAT?)
L108          1 S L87 AND  L92
L109         25 S (L29 OR ?HEPAR!N?) AND L92
```

6 cites

7 cites using some controlled terminology

4 cites

3 cites

13 cites

3 cites

L87 – L113 is directed to searching for the composition

L110	14	S L109 AND (L88 OR L104 OR VLMWH)
L111	2	S L110 AND (XA OR IA OR L90-91)
L112	1	S L111 NOT L34 1 cite
L113	12	S L110 NOT L111 12 cites

KRISHNAN 09/909,797 Inventor Search

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=> d his

     (FILE 'HOME' ENTERED AT 14:20:46 ON 20 JUN 2002)

     FILE 'HCAPLUS' ENTERED AT 14:20:54 ON 20 JUN 2002
L1             3 S PECQUET C?/AU
L2            78 S PERRIN E?/AU
L3           844 S DIAZ J?/AU
L4             7 S VISKOV C?/AU
L5           927 S L1-4
L6             5 S L5 AND HEPARIN
L7             1 S L6 AND METAL
                 SELECT L7 1 RN

     FILE 'REGISTRY' ENTERED AT 14:23:38 ON 20 JUN 2002
L8             9 S E1-9

     FILE 'HCAPLUS' ENTERED AT 14:23:44 ON 20 JUN 2002
L9             1 S L7 AND L8  1 cite w/ 9 cpds displayed
L10            4 S L6 NOT L9
                 SELECT RN L10 1-4

     FILE 'REGISTRY' ENTERED AT 14:27:02 ON 20 JUN 2002
L11           42 S E10-51

     FILE 'HCAPLUS' ENTERED AT 14:27:28 ON 20 JUN 2002
L12            4 S L10 AND L11  4 cites
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priority document

KRISHNAN 09/909,797

=> d ibib abs hitstr

L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:90113 HCAPLUS
DOCUMENT NUMBER: 136:153008
TITLE: **Heparin**-derived polysaccharide mixtures, preparation method and pharmaceutical compositions containing same
INVENTOR(S): **Diaz, Jacques; Pecquet, Christelle ; Perrin, Elisabeth; Viskov, Christian**
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

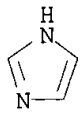
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008295	A1	20020131	WO 2001-FR2332	20010718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2811992	A1	20020125	FR 2000-9572	20000721
US 2002055621	A1	20020509	US 2001-909797	20010723

PRIORITY APPLN. INFO.: FR 2000-9572 A 20000721
US 2000-229123P P 20000831
OTHER SOURCE(S): MARPAT 136:153008

AB The invention concerns **heparin**-derived polysaccharide mixts. having mol. wt. 1500-3000, anti-Xa activity 100-150 UI/mg, anti IIa activity 0-10 UI/mg, anti-Xa activity/anti-IIa activity >10, 2-26 saccharide groups, 4,5-glucuronic 2-O-sulfate terminal groups, under alkali or alk.-earth **metal** salt form. These mixts. are manufd. by depolymn. of quaternary ammonium salts of benzyl esters of **heparin** in org. solvent using a strong org. base having pKa >20 or Na imidazolate, transforming the resulting quaternary ammonium salt of the depolymd. benzylic ester to the Na salt, and sapon. of the ester.

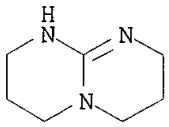
IT **5587-42-8**, Sodium imidazolate **5807-14-7**, 1,5,7-Triazabicyclo[4.4.0]dec-5-ene **81675-81-2** **98015-45-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(depolymn. agent; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)

RN 5587-42-8 HCAPLUS
CN 1H-Imidazole, sodium salt (9CI) (CA INDEX NAME)

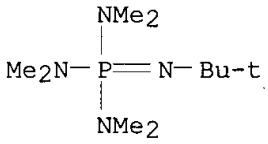


Na

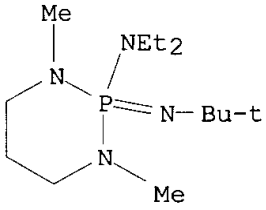
RN 5807-14-7 HCAPLUS
CN 2H-Pyrimido[1,2-a]pyrimidine, 1,3,4,6,7,8-hexahydro- (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 81675-81-2 HCAPLUS
CN Phosphorimidic triamide, N'''-(1,1-dimethylethyl)-N,N,N',N',N'',N''-hexamethyl- (9CI) (CA INDEX NAME)



RN 98015-45-3 HCAPLUS
CN 1,3,2-Diazaphosphorin-2(1H)-amine, 2-[(1,1-dimethylethyl)imino]-N,N-diethyl-2,2,3,4,5,6-hexahydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



IT **81523-64-0DP**, depolymd., sapond.
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(**heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
RN 81523-64-0 HCAPLUS
CN Heparin, phenylmethyl ester, ion (neg.), N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]benzenemethanaminium (9CI) (CA INDEX NAME)

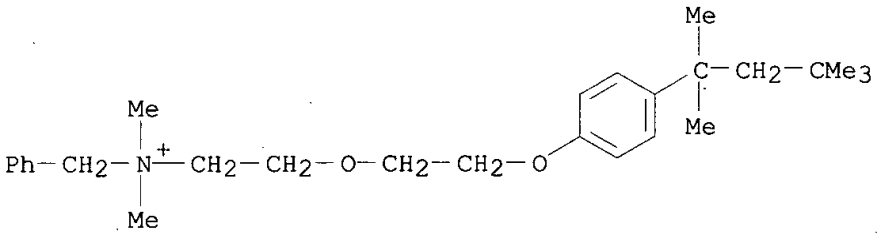
CM 1

CRN 81405-95-0
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 10172-60-8
CMF C27 H42 N O2



IT **50732-58-6P**, preparation **81523-64-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(precursor; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
RN 50732-58-6 HCAPLUS
CN Heparin, ion (neg.), N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]benzenemethanaminium (9CI) (CA INDEX NAME)

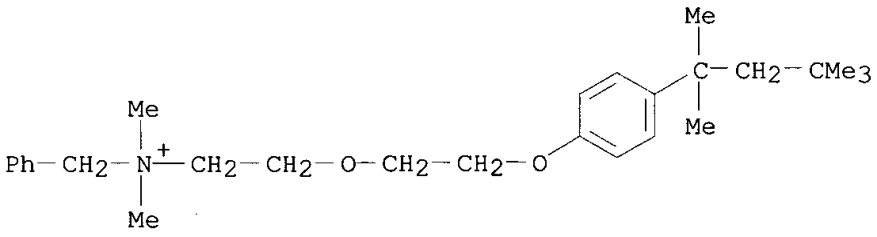
CM 1

CRN 51053-42-0
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 10172-60-8
CMF C27 H42 N O2



RN 81523-64-0 HCAPLUS
CN Heparin, phenylmethyl ester, ion (neg.), N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-

tetramethylbutyl)phenoxy]ethoxy]ethyl]benzenemethanaminium (9CI) (CA INDEX NAME)

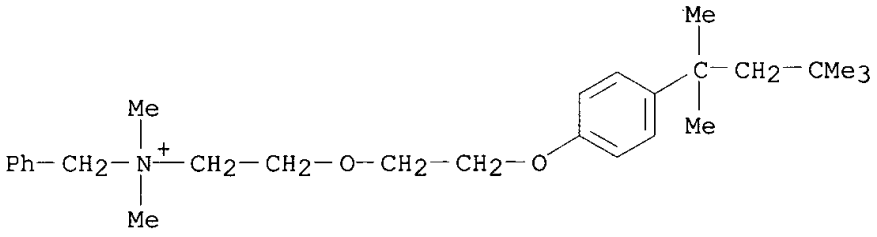
CM 1

CRN 81405-95-0
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

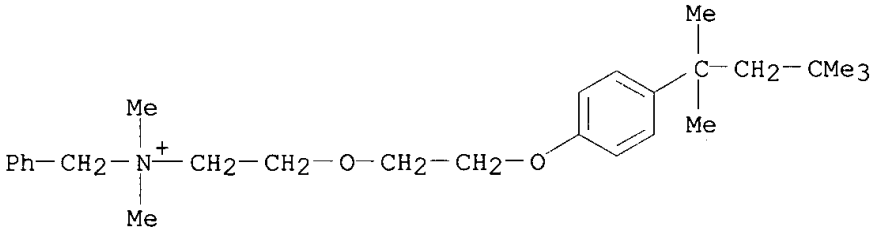
CM 2

CRN 10172-60-8
CMF C27 H42 N O2



IT **100-44-7**, Benzyl chloride, reactions **121-54-0**, Benzethonium chloride **81209-41-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
RN 100-44-7 HCAPLUS
CN Benzene, (chloromethyl)- (9CI) (CA INDEX NAME)

RN 121-54-0 HCAPLUS
CN Benzenemethanaminium, N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]-, chloride (9CI) (CA INDEX NAME)



RN 81209-41-8 HCAPLUS

CN Heparin, phenylmethyl ester, sodium salt (9CI) (CA INDEX NAME)

CM 1

CRN 9005-49-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 100-51-6
CMF C7 H8 O

HO—CH_2—Ph

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind

L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
ICS A61K031-727
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 1, 63
ST benzyl ester **heparin** quaternary ammonium salt depolymn strong base; anticoagulant activity enhanced depolymd **heparin**; antithrombic activity enhanced depolymd **heparin**
IT Phosphazenes
RL: RCT (Reactant); RACT (Reactant or reagent)
(depolymn. agent; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
IT Anticoagulants
(**heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
IT Polysaccharides, preparation
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(**heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
IT **5587-42-8**, Sodium imidazolate **5807-14-7**, 1,5,7-Triazabicyclo[4.4.0]dec-5-ene **81675-81-2** **98015-45-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(depolymn. agent; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
IT **81523-64-0DP**, depolymd., sapond.
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(**heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)
IT **50732-58-6P**, preparation **81523-64-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(precursor; **heparin**-derived polysaccharide mixts. with

improved anticoagulant and antithrombic activity)

IT **100-44-7**, Benzyl chloride, reactions **121-54-0**, Benzethonium chloride **81209-41-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; **heparin**-derived polysaccharide mixts. with improved anticoagulant and antithrombic activity)

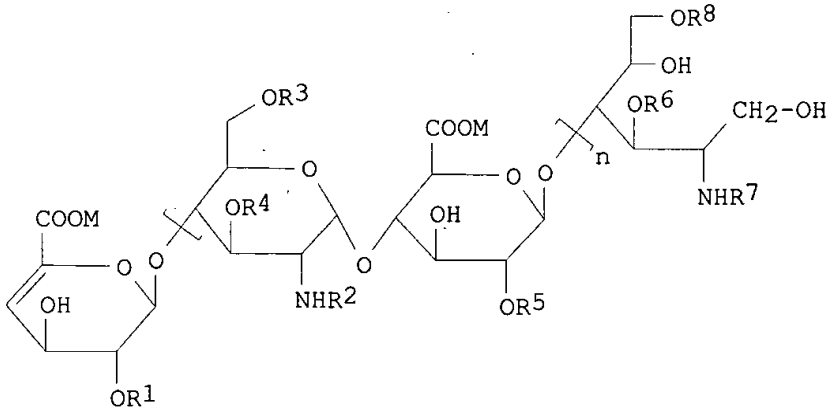
applicant's related work

=> d ibib abs hitstr 1

L10 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:730755 HCAPLUS
DOCUMENT NUMBER: 135:273169
TITLE: Preparation of uronic acid-containing oligosaccharides as antiinflammatory agents
INVENTOR(S): Mourier, Pierre; **Perrin, Elisabeth**; **Viskov, Christian**
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072762	A1	20011004	WO 2001-FR903	20010326
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
FR 2807043	A1	20011005	FR 2000-3910	20000328
US 2002019368	A1	20020214	US 2001-817428	20010326

PRIORITY APPLN. INFO.: FR 2000-3910 A 20000328
OTHER SOURCE(S): MARPAT 135:273169
GI



I

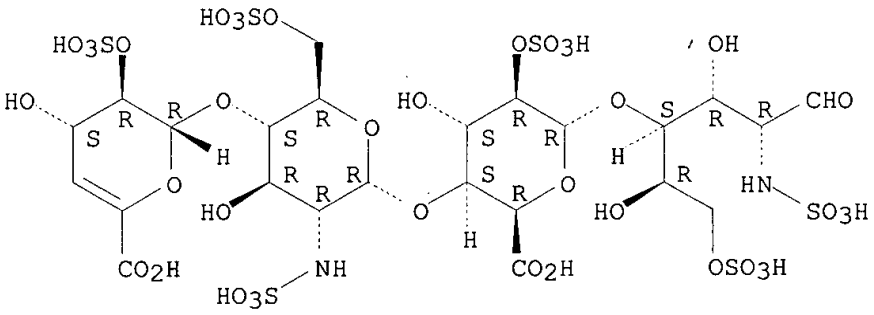
AB Uronic acid-contg. oligosaccharides I (n = 0-25; R1, R3-R6, R8 are independently H, SO3M; R2, R7 independently H, SO3M, COMe; M is Na, Ca, Mg, K, oligosaccharide) were prepd. from **heparin** as antiinflammatory agents. Thus, I (n = 1; R1-R3 = R5 = R7-R8 = SO3Na; R4 =

R6 = H) was prepd. and tested in mice as antiinflammatory agent.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d hitstr 1

L12 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS
IT **96849-33-1P 333796-83-1P 333796-84-2P**
333796-85-3P 363148-40-7P 363148-42-9P
363148-43-0P 363148-44-1P 363148-45-2P
363148-48-5P 363148-49-6P 363148-51-0P
363148-52-1P 363148-53-2P 363595-83-9P
363595-85-1P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of uronic acid-contg. oligosaccharides from **heparin** as antiinflammatory agents)
RN 96849-33-1 HCAPLUS
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), octasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

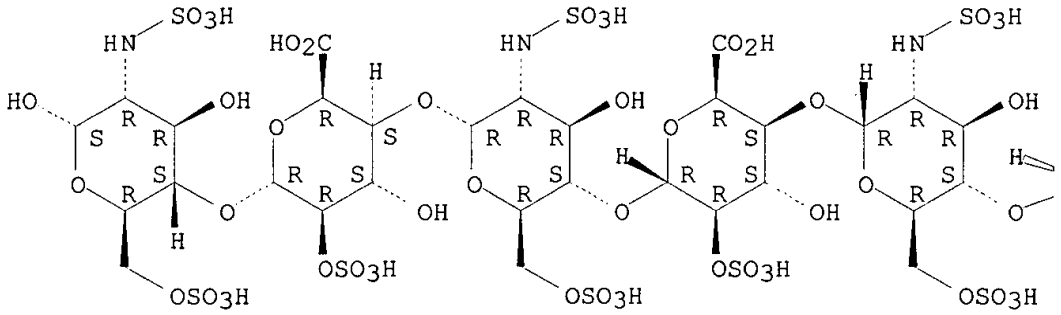


●8 Na

RN 333796-83-1 HCAPLUS
CN .alpha.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

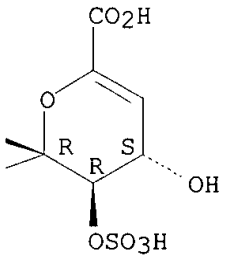
Absolute stereochemistry.

PAGE 1-A



●12 Na

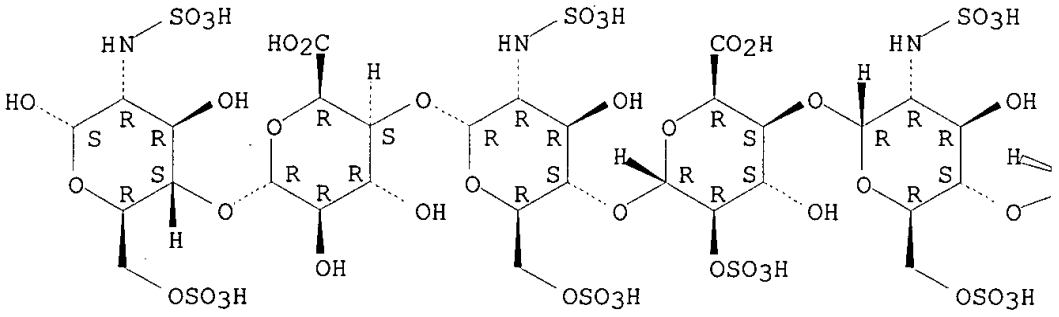
PAGE 1-B



RN 333796-84-2 HCAPLUS
CN .alpha.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), undecasodium salt (9CI) (CA INDEX NAME)

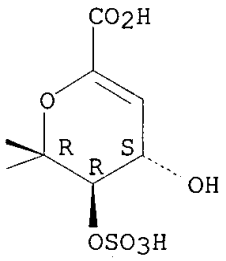
Absolute stereochemistry.

PAGE 1-A



●11 Na

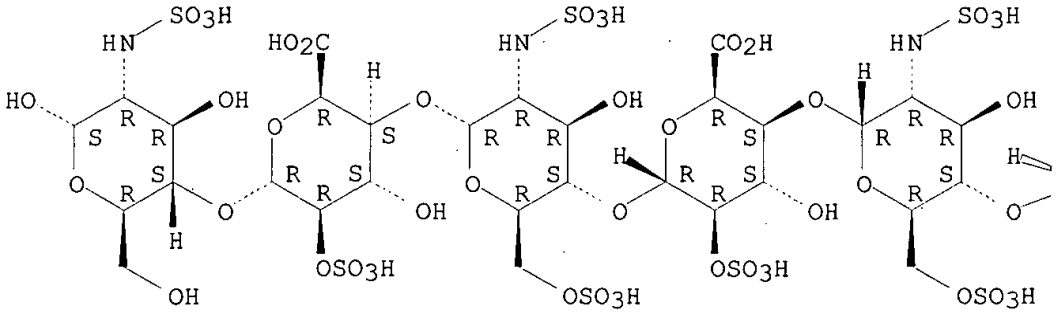
PAGE 1-B



RN 333796-85-3 HCAPLUS
CN .alpha.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, undecasodium salt (9CI) (CA INDEX NAME)

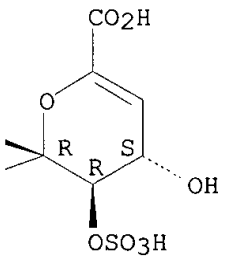
Absolute stereochemistry.

PAGE 1-A



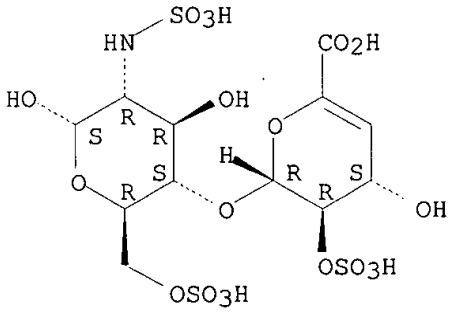
●11 Na

PAGE 1-B



RN 363148-40-7 HCAPLUS
CN .alpha.-D-Glucopyranose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

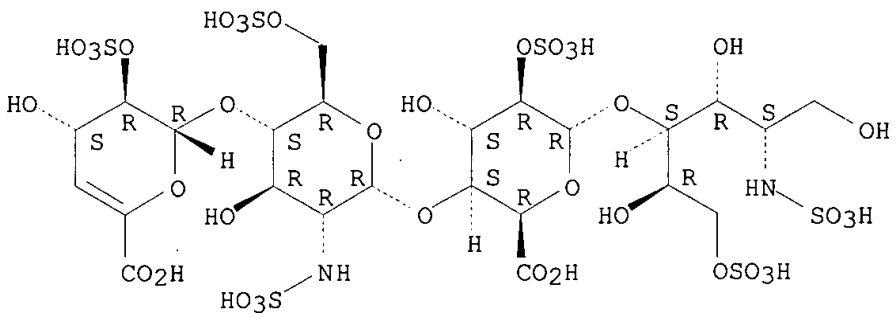
Absolute stereochemistry.



4 Na

RN 363148-42-9 HCAPLUS
CN D-Glucitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), octasodium salt (9CI) (CA INDEX NAME)

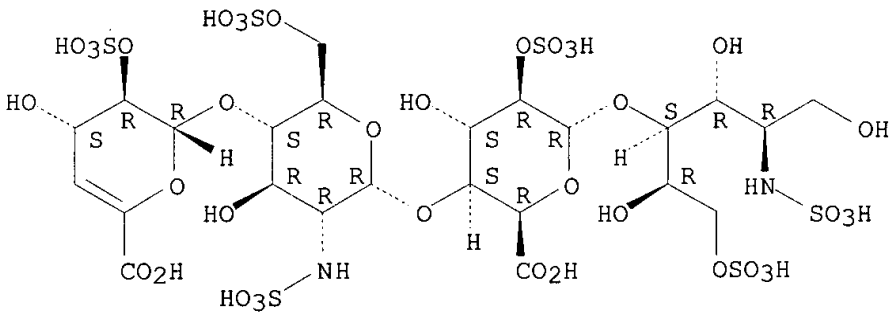
Absolute stereochemistry.



●8 Na

RN 363148-43-0 HCAPLUS
CN D-Mannitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), octasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

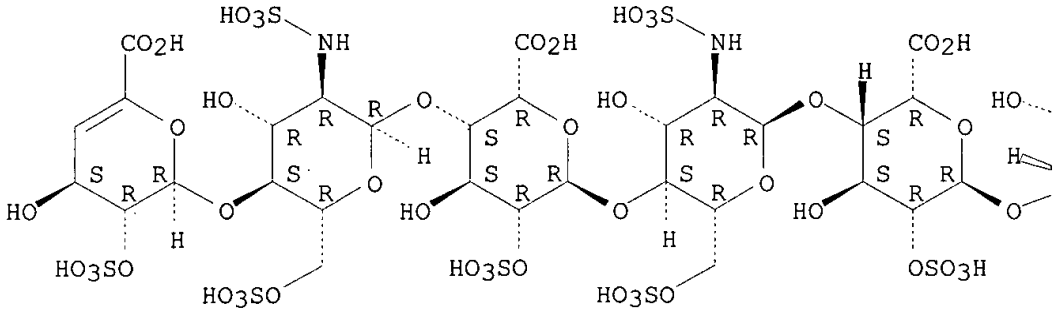


●8 Na

RN 363148-44-1 HCAPLUS
CN D-Glucitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

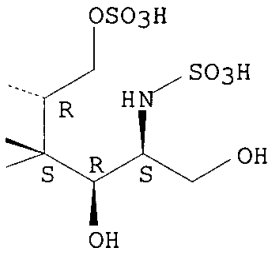
Absolute stereochemistry.

PAGE 1-A



●12 Na

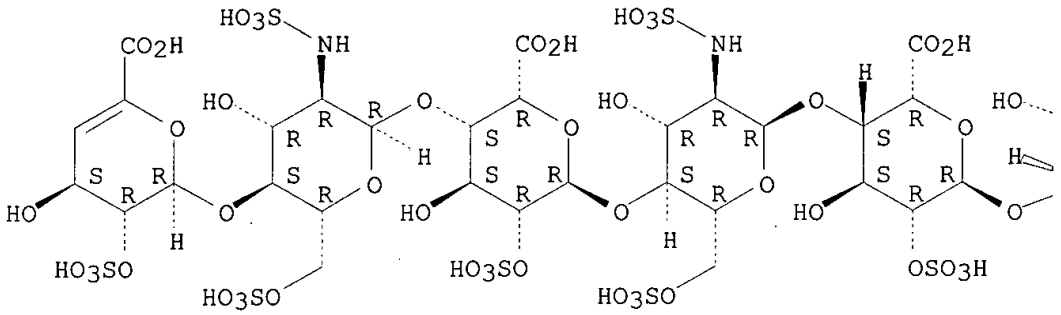
PAGE 1-B



RN 363148-45-2 HCAPLUS
CN D-Mannitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

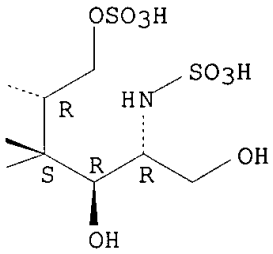
Absolute stereochemistry.

PAGE 1-A



●12 Na

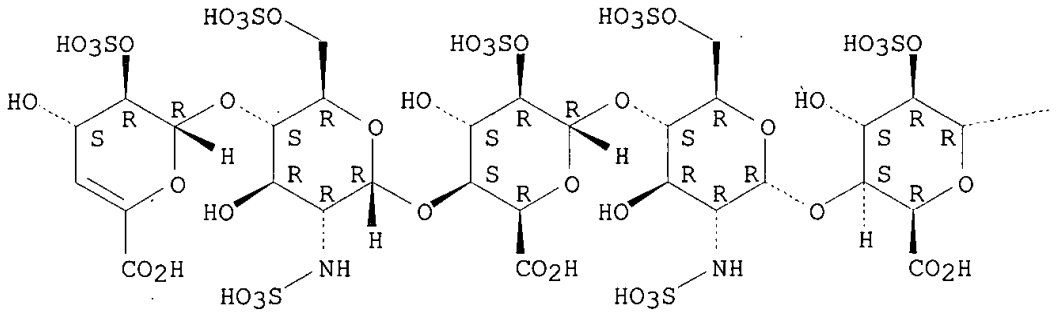
PAGE 1-B



RN 363148-48-5 HCAPLUS
CN D-Glucitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), hexadecasodium salt (9CI) (CA INDEX NAME)

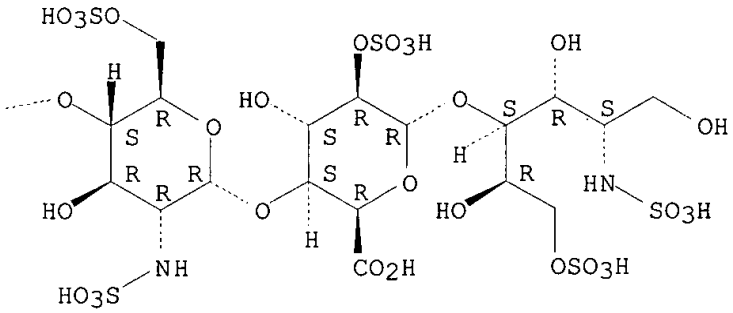
Absolute stereochemistry.

PAGE 1-A



●16 Na

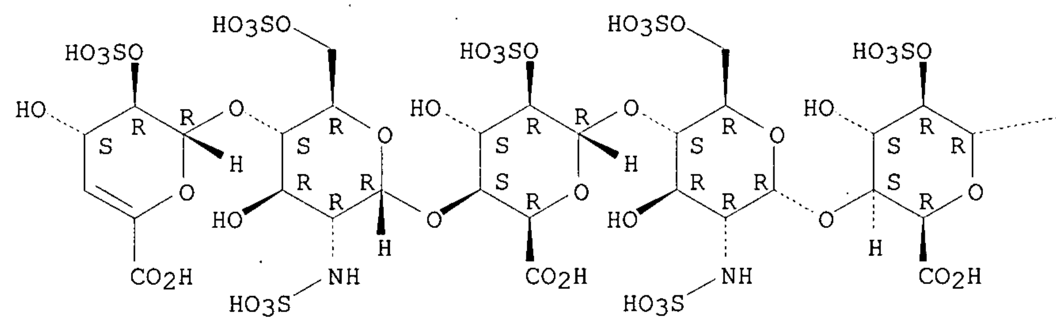
PAGE 1-B



RN 363148-49-6 HCAPLUS
CN D-Mannitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), hexadecasodium salt (9CI) (CA INDEX NAME)

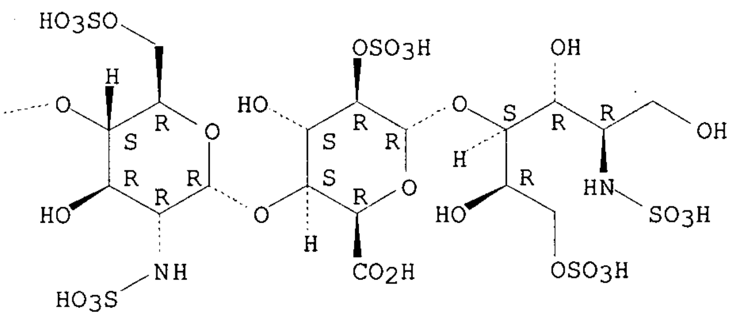
Absolute stereochemistry.

PAGE 1-A



●16 Na

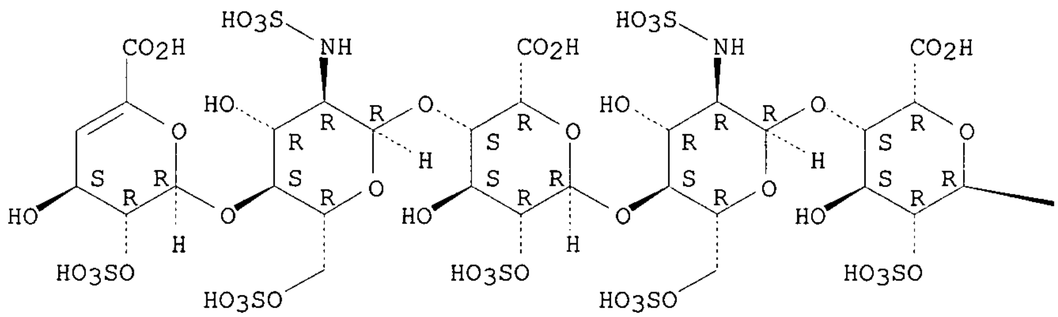
PAGE 1-B



RN 363148-51-0 HCAPLUS
CN D-Mannose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), eicosasodium salt (9CI) (CA INDEX NAME)

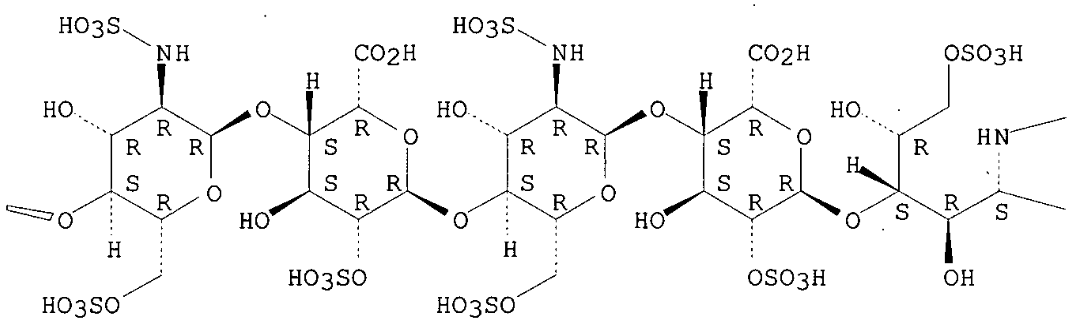
Absolute stereochemistry.

PAGE 1-A

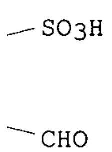


●20 Na

PAGE 1-B



PAGE 1-C



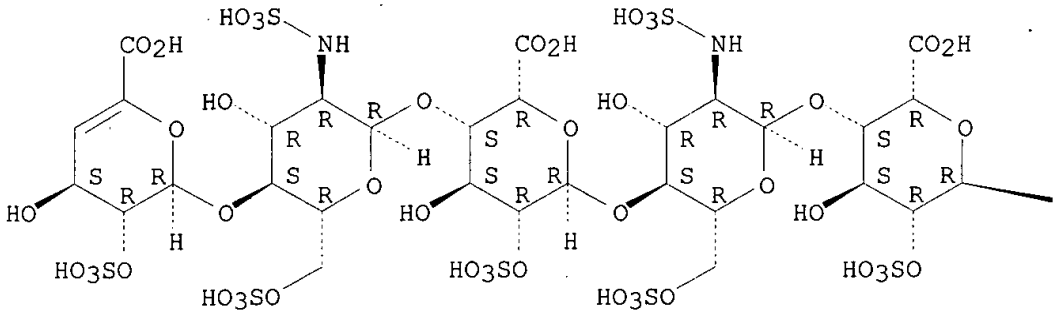
RN 363148-52-1 HCAPLUS

CN D-Glucitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), eicosasodium

salt (9CI) (CA INDEX NAME)

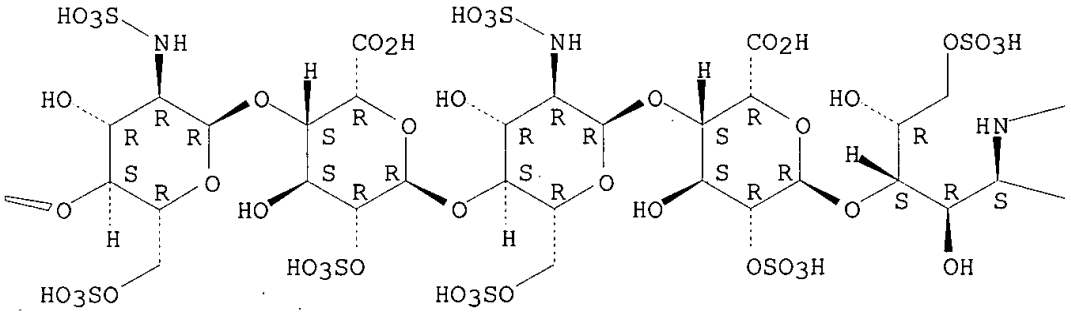
Absolute stereochemistry.

PAGE 1-A

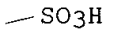


●20 Na

PAGE 1-B



PAGE 1-C



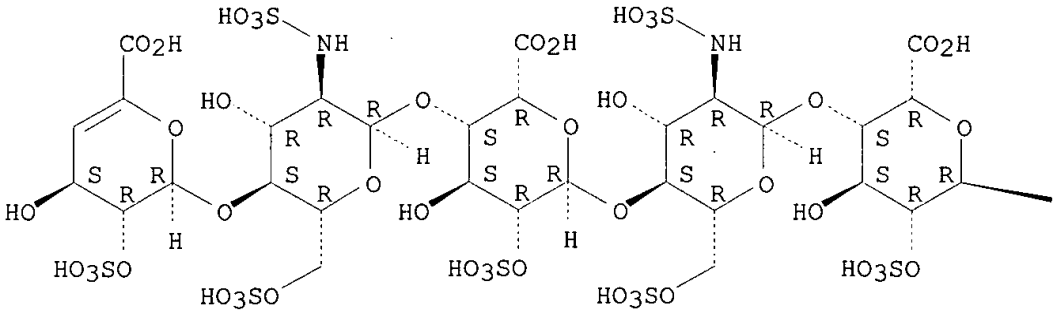
RN 363148-53-2 HCAPLUS

CN D-Mannitol, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-

idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), eicosasodium salt (9CI) (CA INDEX NAME)

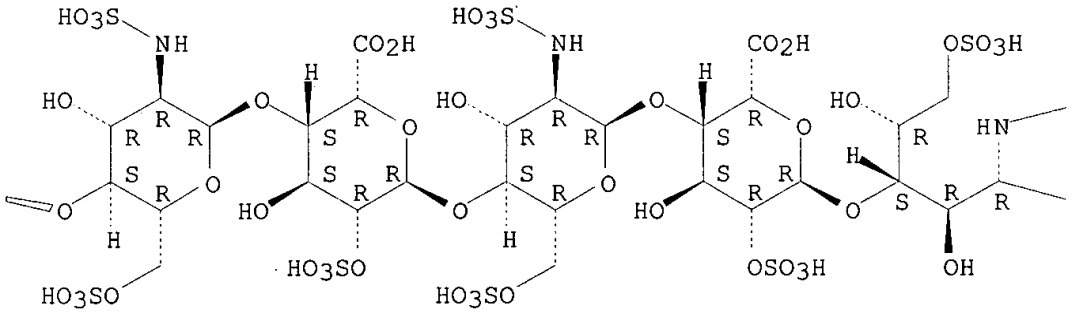
Absolute stereochemistry.

PAGE 1-A

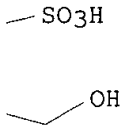


●20 Na

PAGE 1-B

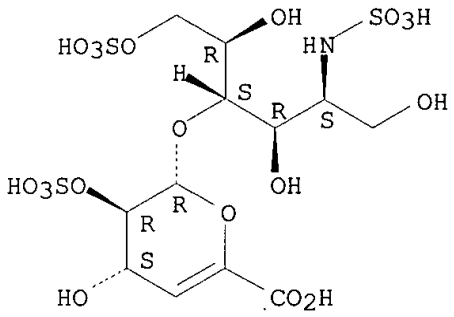


PAGE 1-C



RN 363595-83-9 HCAPLUS
CN D-Glucitol, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

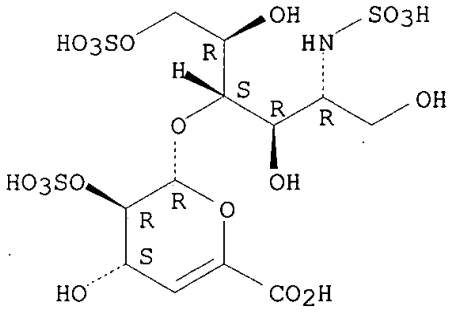
Absolute stereochemistry.



●4 Na

RN 363595-85-1 HCAPLUS
CN D-Mannitol, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●4 Na

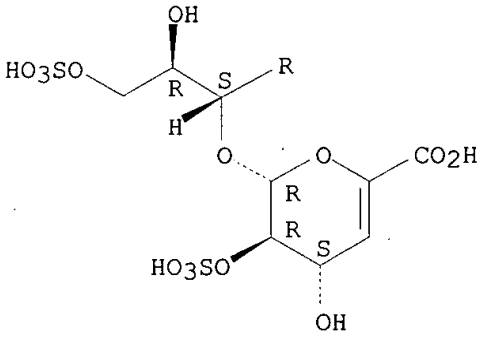
IT **9025-39-2**, Heparinase I
RL: CAT (Catalyst use); USES (Uses)
(prepn. of uronic acid-contg. oligosaccharides from **heparin** as antiinflammatory agents)
RN 9025-39-2 HCAPLUS
CN Lyase, heparin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9005-49-6, Heparin**, reactions **136098-10-7 161729-25-5 164082-52-4 164082-54-6 340154-98-5 340156-51-6 363148-41-8 363148-47-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of uronic acid-contg. oligosaccharides from **heparin** as antiinflammatory agents)
RN 9005-49-6 HCAPLUS

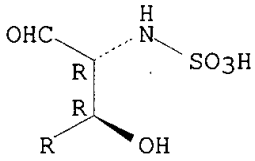
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 136098-10-7 HCAPLUS
CN D-Glucose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



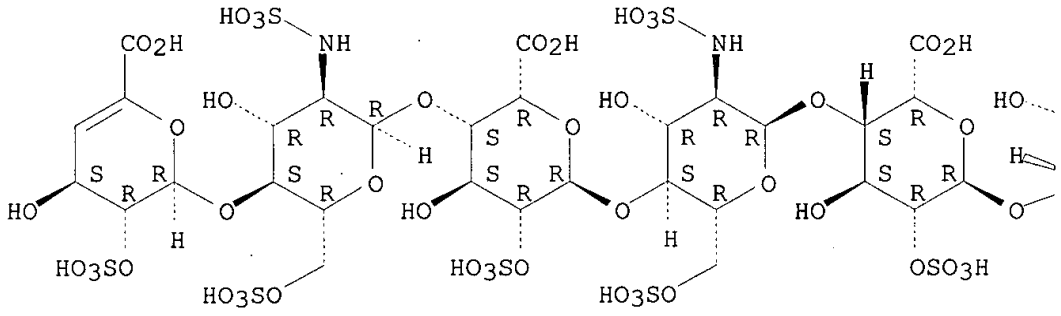
● 4 Na



RN 161729-25-5 HCAPLUS
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

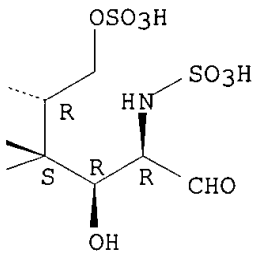
Absolute stereochemistry.

PAGE 1-A



12 Na

PAGE 1-B



RN 164082-52-4 HCAPLUS
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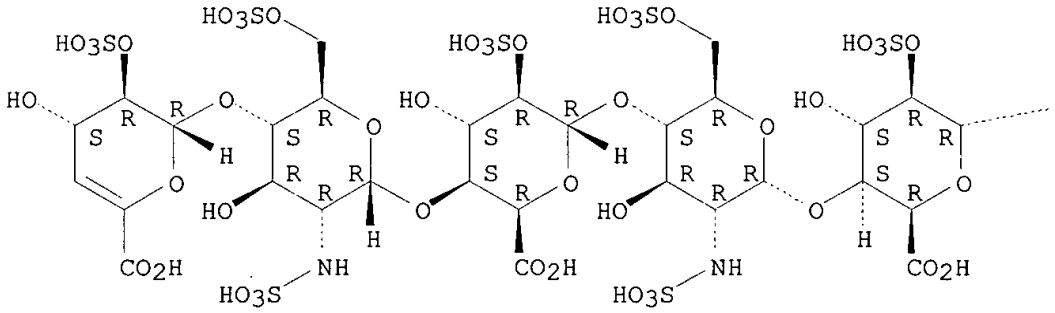
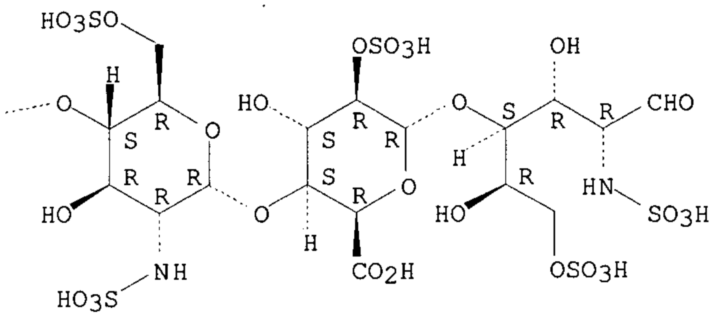
Absolute stereochemistry.

PAGE 1-A



●16 Na

PAGE 1-B



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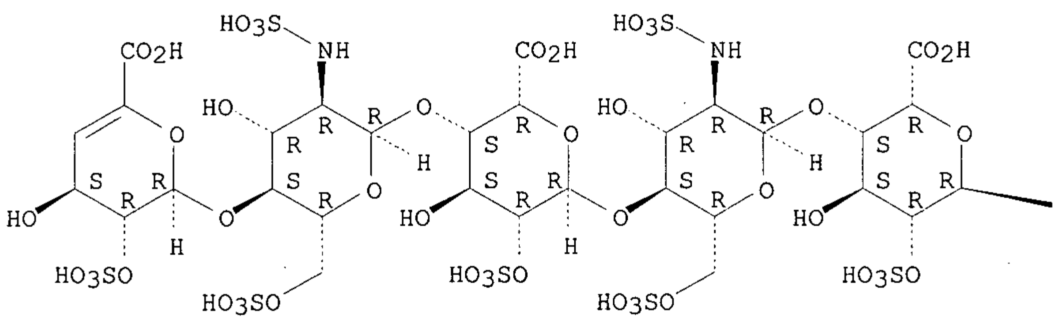
CN D-Glucose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), eicosasodium salt (9CI) (CA INDEX NAME)

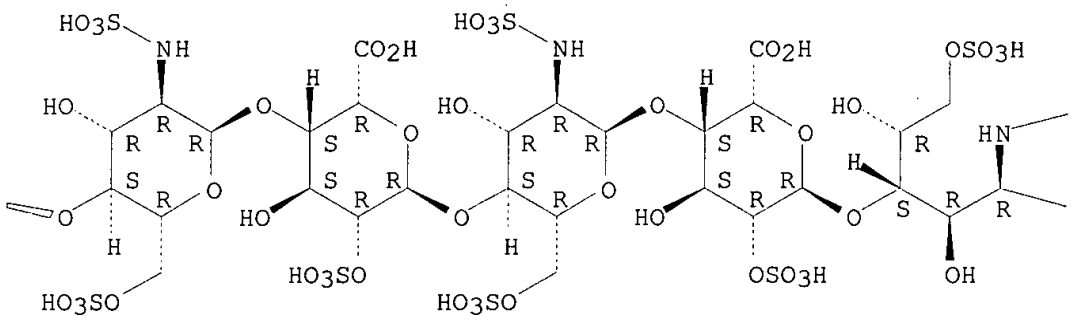
Absolute stereochemistry.

PAGE 1-A



●20 Na

PAGE 1-B



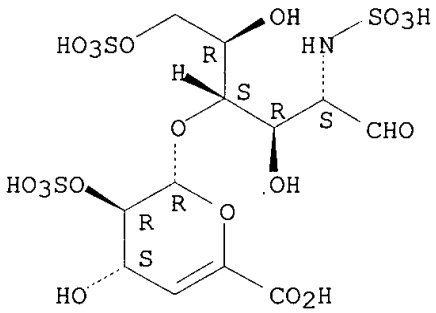
PAGE 1-C

SO3H

CHO

RN 340154-98-5 HCAPLUS
CN D-Mannose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●4 Na

RN 340156-51-6 HCAPLUS
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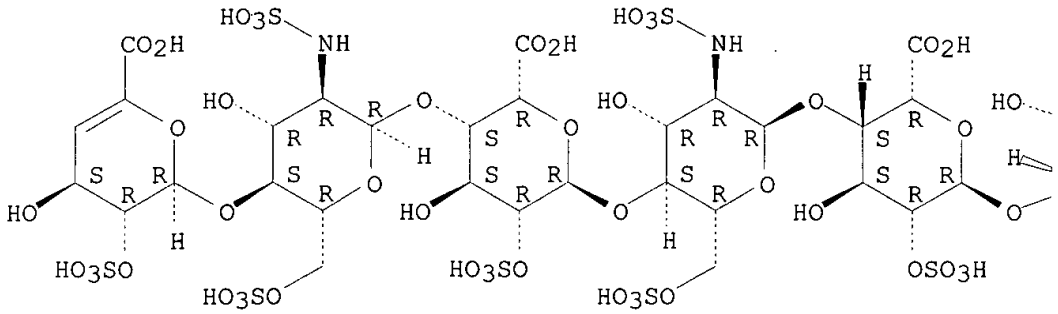
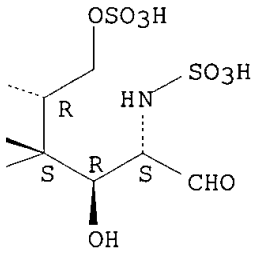
Absolute stereochemistry.

PAGE 1-A



●12 Na

PAGE 1-B



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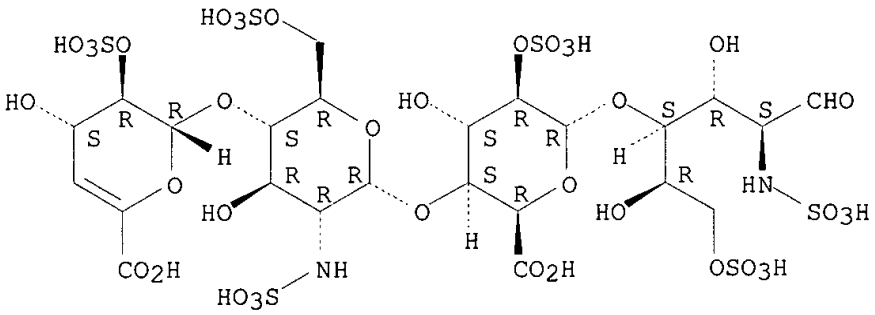
Absolute stereochemistry.

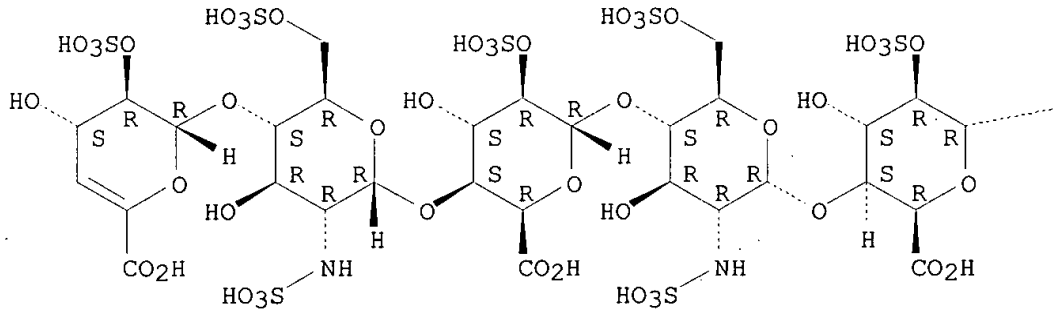


●8 Na

RN 363148-47-4 HCAPLUS
CN D-Mannose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), hexadecasodium salt (9CI) (CA INDEX NAME)

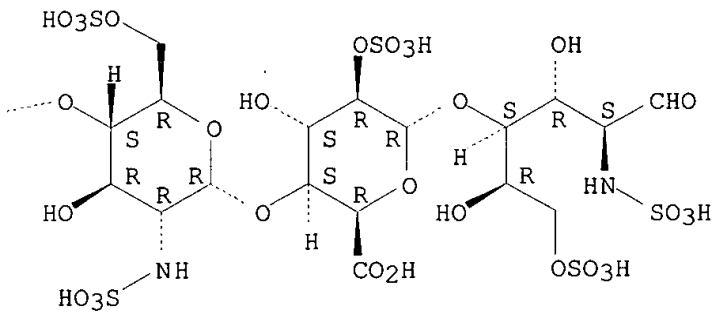
Absolute stereochemistry.

PAGE 1-A



●16 Na

PAGE 1-B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CO2H
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HN
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OH
OSO3H

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L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:300732 HCAPLUS
DOCUMENT NUMBER: 134:281073
TITLE: Preparation of uronic acid-containing oligosaccharides as antiinflammatory agents
INVENTOR(S): Mourier, Pierre; **Perrin, Elisabeth**; **Viskov, Christian**; Stutzmann, Jean-marie; Wahl, Florence
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029055	A2	20010426	WO 2000-FR2897	20001018
WO 2001029055	A3	20020214		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2800074	A1	20010427	FR 1999-13182	19991022
FR 2800074	B1	20011221		

PRIORITY APPLN. INFO.: FR 1999-13182 A 19991022
OTHER SOURCE(S): CASREACT 134:281073; MARPAT 134:281073
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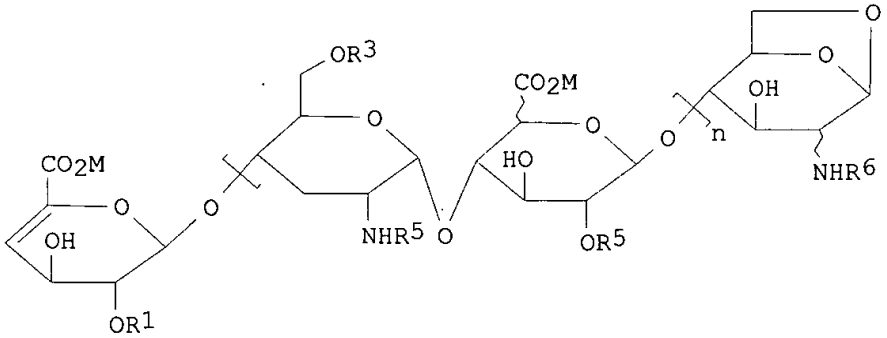


I

AB The invention concerns oligosaccharides I wherein n is 0-25; R1, R3-R5 are identical or different and represent H, SO3M; R2, R6 are identical or different and represent H, SO3M, COMe; M is Na, Ca, Mg, K; their diastereomers, methods for prepg. them as antiinflammatory agents. Thus,.

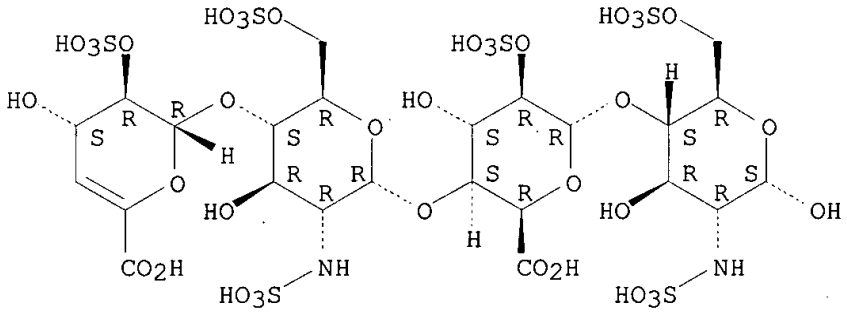
4-Deoxy-2-O-sulfoanda-L-threo-hex-4-enopyranosyluronate-(1-4)-2-deoxy-2-sulfoamino-6-O-sulfo-D-glucopyranosyl-(1-4)-2-O-sulfo-aX-L-idopyranosyluronate-(1-4)-2-deoxy-2-sulfoamino-6-O-sulfo-D-glucopyranosyl-(1-4)-O-sulfo-ca-L-idopyranosyluronate-(1-4)-1,6-anhydro-2-deoxy-2-sulfoamino-3-D-glucopyranose undeca-sodium salt was prepd. and tested in rats as antiinflammatory agent.

IT **98797-51-4P 333796-82-0P 333796-83-1P 333796-84-2P 333796-85-3P 333796-86-4P 333796-87-5P 333796-88-6P 333796-89-7P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of uronic acid-contg. oligosaccharides as antiinflammatory agents)

RN 98797-51-4 HCAPLUS

CN .alpha.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), octasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

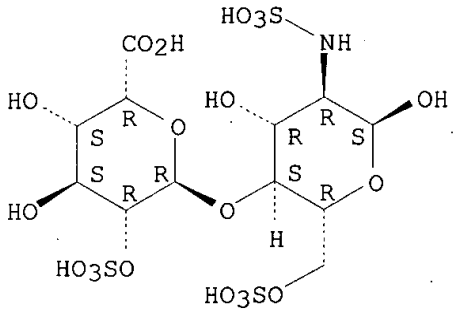


●8 Na

RN 333796-82-0 HCAPLUS

CN .alpha.-D-Glucopyranose, 2-deoxy-2-(sulfoamino)-4-O-(2-O-sulfo-.alpha.-L-idopyranuronosyl)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

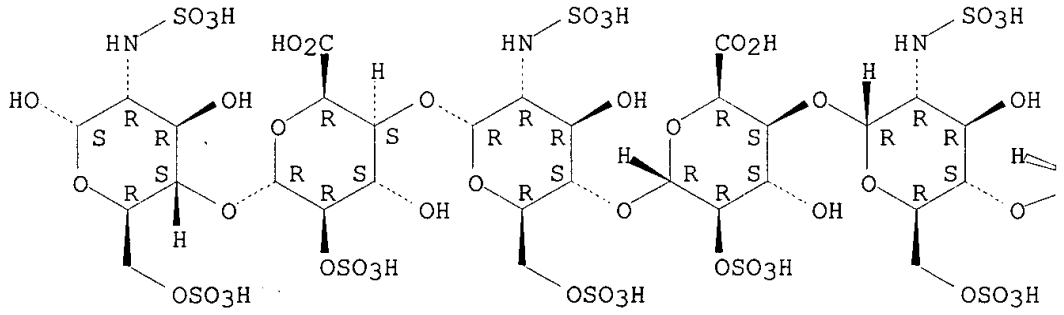


●4 Na

RN 333796-83-1 HCAPLUS
CN .alpha.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

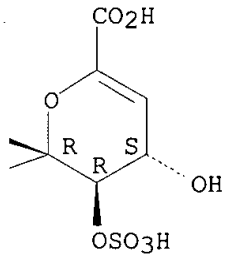
Absolute stereochemistry.

PAGE 1-A



●12 Na

PAGE 1-B



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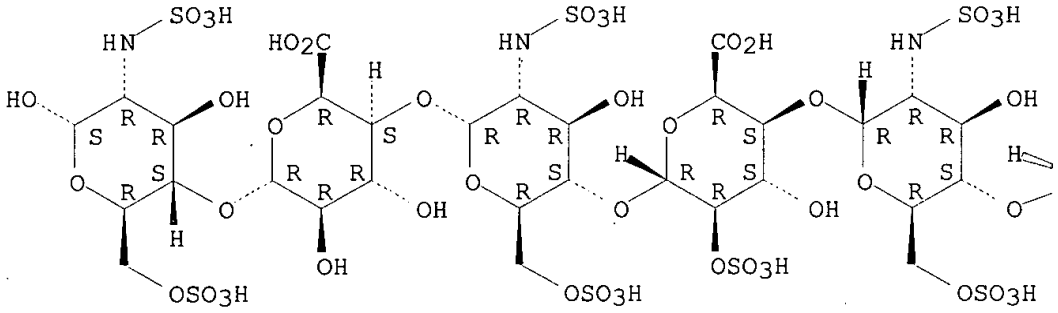
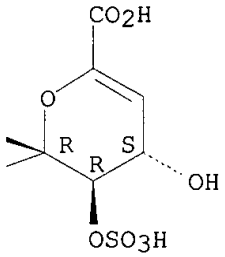
Absolute stereochemistry.

PAGE 1-A



●11 Na

PAGE 1-B



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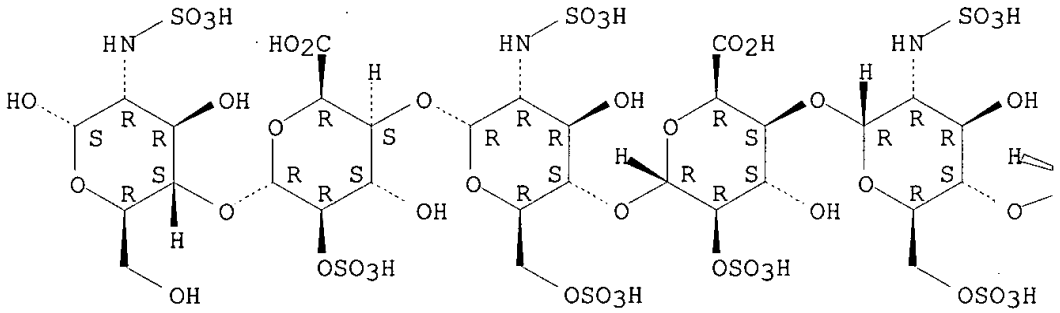
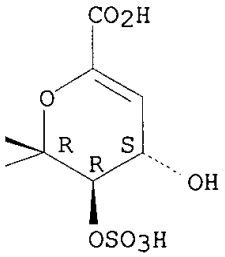
Absolute stereochemistry.

PAGE 1-A



●11 Na

PAGE 1-B



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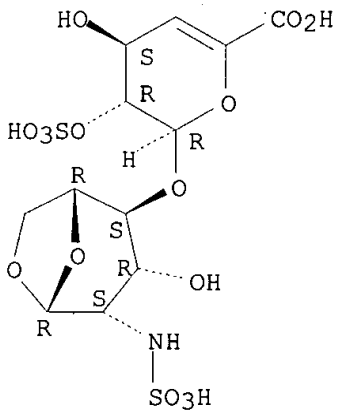
Absolute stereochemistry.



●3 Na

RN 333796-87-5 HCAPLUS
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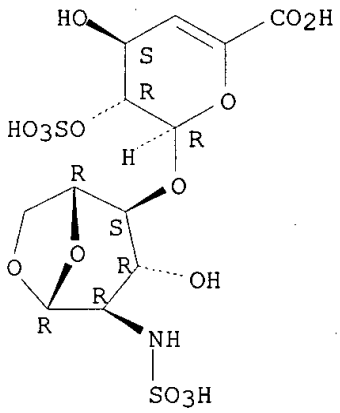
Absolute stereochemistry.



●3 Na

RN 333796-88-6 HCAPLUS
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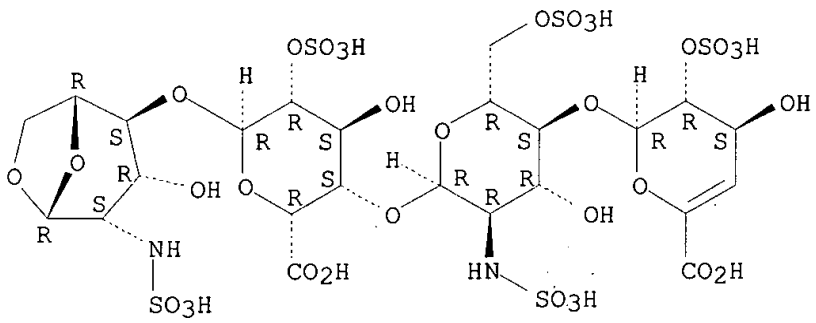
glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-1,6-anhydro-2-deoxy-2-(sulfoamino)-, heptasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●7 Na

RN 333796-89-7 HCAPLUS
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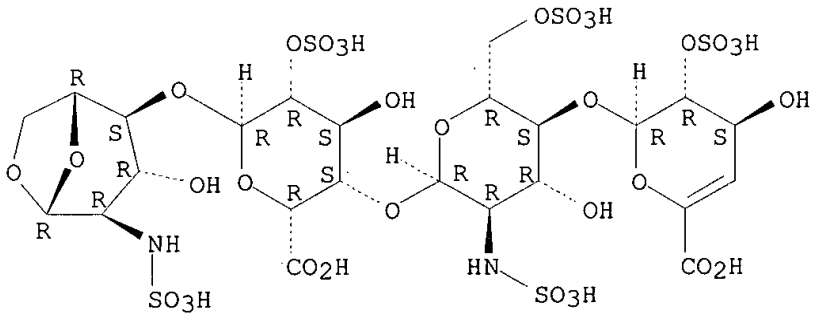
Absolute stereochemistry.



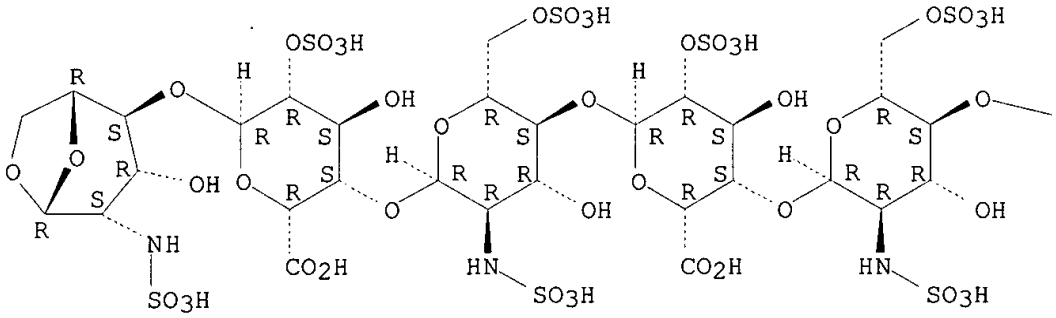
●7 Na

IT **333796-90-0P 333796-91-1P 333796-92-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of uronic acid-contg. oligosaccharides as antiinflammatory agents)
RN 333796-90-0 HCAPLUS
CN .beta.-D-Mannopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-

glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-1,6-anhydro-2-deoxy-2-(sulfoamino)-, undecasodium salt (9CI) (CA INDEX NAME)

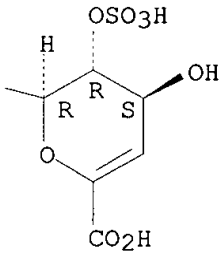
Absolute stereochemistry.

PAGE 1-A



●11 Na

PAGE 1-B

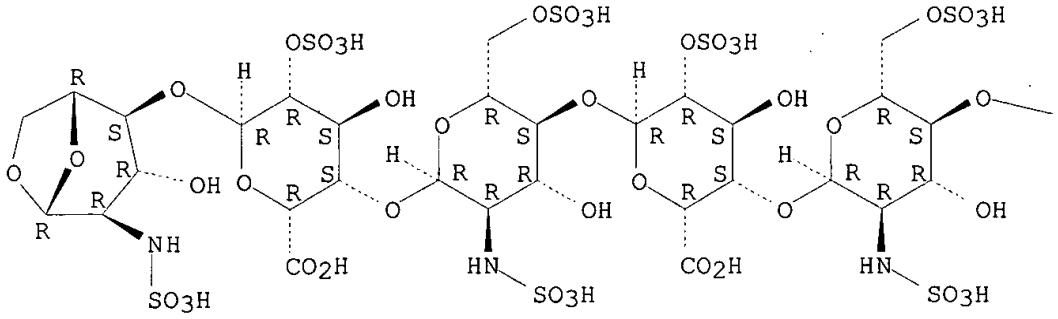


RN 333796-91-1 HCAPLUS

CN .beta.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-1,6-anhydro-2-deoxy-2-(sulfoamino)-, undecasodium salt (9CI) (CA INDEX NAME)

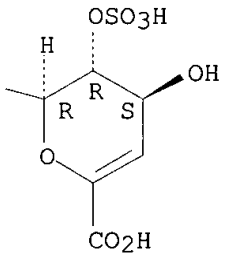
Absolute stereochemistry.

PAGE 1-A



●11 Na

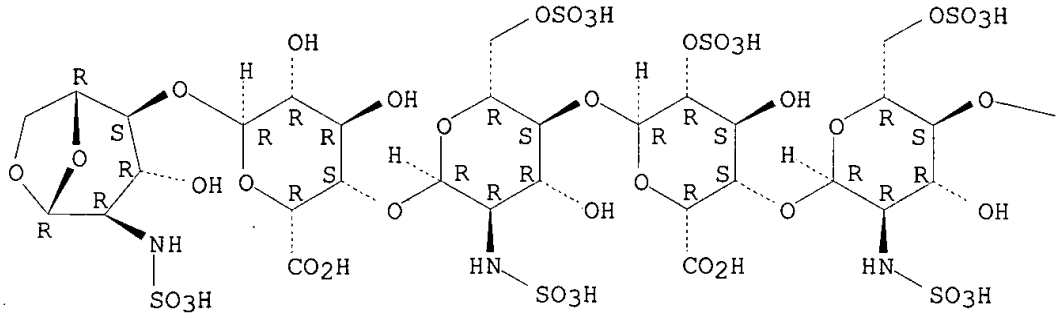
PAGE 1-B



RN 333796-92-2 HCAPLUS
CN .beta.-D-Glucopyranose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-1,6-anhydro-2-deoxy-2-(sulfoamino)-, decasodium salt (9CI) (CA INDEX NAME)

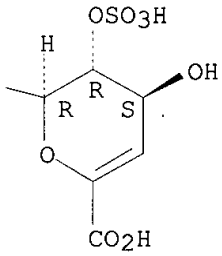
Absolute stereochemistry.

PAGE 1-A



●10 Na

PAGE 1-B

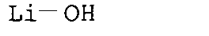


IT **9025-39-2**, Heparinase I
RL: CAT (Catalyst use); USES (Uses)
(prepn. of uronic acid-contg. oligosaccharides as antiinflammatory agents)
RN 9025-39-2 HCAPLUS
CN Lyase, heparin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **1310-58-3**, Potassium hydroxide, reactions **1310-65-2**, Lithium hydroxide **1310-73-2**, Sodium hydroxide, reactions **2052-49-5**, Tetrabutylammonium hydroxide **9005-49-6**, **Heparin**, reactions **21351-79-1**, Cesium hydroxide **340154-98-5 340156-51-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of uronic acid-contg. oligosaccharides as antiinflammatory agents)
RN 1310-58-3 HCAPLUS
CN Potassium hydroxide (K(OH)) (9CI) (CA INDEX NAME)

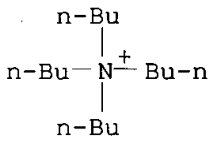
K—OH

RN 1310-65-2 HCAPLUS
CN Lithium hydroxide (Li(OH)) (9CI) (CA INDEX NAME)



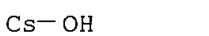
RN 1310-73-2 HCAPLUS
CN Sodium hydroxide (Na(OH)) (9CI) (CA INDEX NAME)

RN 2052-49-5 HCAPLUS
CN 1-Butanaminium, N,N,N-tributyl-, hydroxide (9CI) (CA INDEX NAME)



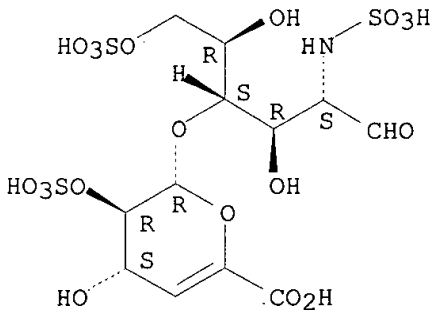
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 21351-79-1 HCAPLUS
CN Cesium hydroxide (Cs(OH)) (9CI) (CA INDEX NAME)



RN 340154-98-5 HCAPLUS
CN D-Mannose, 2-deoxy-4-O-(4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl)-2-(sulfoamino)-, 6-(hydrogen sulfate), tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

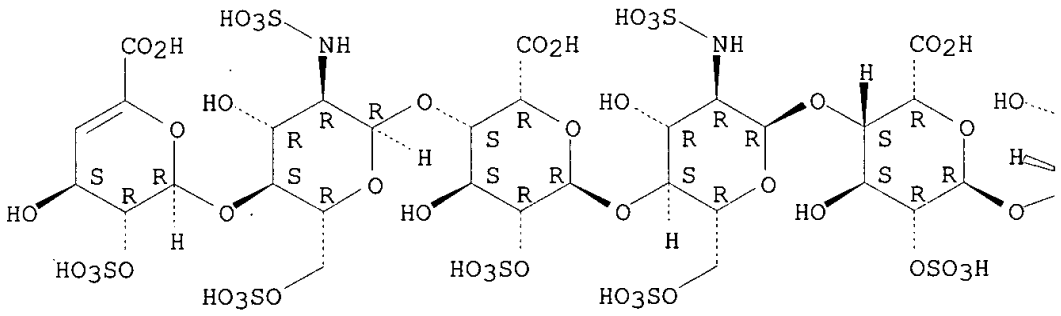


●4 Na

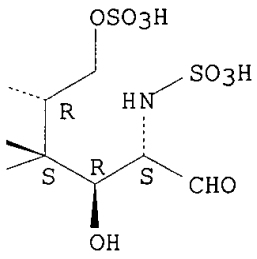
RN 340156-51-6 HCAPLUS
CN D-Mannose, O-4-deoxy-2-O-sulfo-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-O-2-deoxy-6-O-sulfo-2-(sulfoamino)-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-2-O-sulfo-.alpha.-L-idopyranuronosyl-(1.fwdarw.4)-2-deoxy-2-(sulfoamino)-, 6-(hydrogen sulfate), dodecasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●12 Na


OSO3H
SO3H
HN
R
S
R
S
CHO
OH

=> d ibib abs hitstr 3

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:699358 HCAPLUS
DOCUMENT NUMBER: 125:316100
TITLE: A proposed model to monitor **heparin** therapy using the concentrated thrombin time which allows standardization of reagents and improved estimation of **heparin** concentrations
AUTHOR(S): Ray, M. J.; **Perrin, E. J.**; Smith, I. R.; Hawson, G. A. T.
CORPORATE SOURCE: Departments Haematology and Physical Sciences, Prince Charles Hospital, Brisbane, 4032, Australia
SOURCE: Blood Coagulation Fibrinolysis (1996), 7(5), 515-521
CODEN: BLFIE7; ISSN: 0957-5235
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The concd. thrombin time (CTT), a thrombin time performed with a high concn. of thrombin, was evaluated as an alternative to the activated partial thromboplastin time (APTT) for monitoring of **heparin** therapy. Forty-nine plasmas from patients receiving unfractionated **heparin** therapy were tested. It was first demonstrated that CTTs using three com. reagents could be standardized against CTTs performed with a ref. reagent, MRC reagent 66/305. For comparison, APTTs were performed on the plasmas. As a benchmark of the degree of heparinization, the **heparin** concn. of the plasmas was detd. by chromogenic anti-IIa **heparin** assays, therapeutic range being 0.2-0.4 units/mL. The optimal relationships of the CTTs and APTT with the **heparin** concn. were established. These were used to predict the **heparin** concns. of the plasmas from the results of the APTT, CTT performed with the ref. reagent, and transformed CTT performed with each of the three com. reagents. In predicting the assayed plasma **heparin** concns., the accuracy of the APTT was only 53%, while the CTT was from 78 to 82%. The CTT can be standardized and, subject to results of clin. trials, could provide an improved method of monitoring **heparin** therapy.
IT **9002-04-4**, Thrombin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(concd. thrombin time; improved method of monitoring **heparin** therapy)
RN 9002-04-4 HCAPLUS
CN Thrombin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9005-49-6**, **Heparin**, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(improved method of monitoring **heparin** therapy)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 4

L12 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:1984 HCAPLUS
DOCUMENT NUMBER: 112:1984
TITLE: Production in Escherichia coli of a biologically active subfragment of von Willebrand factor corresponding to the platelet glycoprotein Ib, collagen and **heparin** binding domains
AUTHOR(S): Pietu, Genevieve; Meulien, Pierre; Cherel, Ghislaine; **Diaz, Joseph**; Baruch, Dominique; Courtney, Michael; Meyer, Dominique
CORPORATE SOURCE: Hop. Bicetre, Le Kremlin Bicetre, 94275, Fr.
SOURCE: Biochem. Biophys. Res. Commun. (1989), 164(3), 1339-47
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A full-length cDNA for von Willebrand factor (vWF) has been cloned from a human lung cDNA library and a fragment of this cDNA has been modified to allow its expression in E. coli. This fragment, which corresponds to Val 449-Asn 730 of vWF and includes the glycoprotein Ib-binding domain and binding sites for collagen and **heparin**, was subcloned into an expression vector contg. an inducible .lambda. PL promoter. On induction, the expressed recombinant vWF subfragment migrated with a mol. wt. of around 38,000 after SDS-PAGE. It was identified as a vWF fragment by Western blotting using either a polyclonal or a monoclonal antibody which inhibits the binding of vWF to glycoprotein Ib. Following solubilization in urea, the bacterial ext. inhibited ristocetin-induced platelet aggregation and bound to ristocetin-treated platelets, to collagen, and to **heparin**.

IT **109319-16-6**
RL: PRP (Properties)
(human gene for, cloning and expression in Escherichia coli of)
RN 109319-16-6 HCAPLUS
CN Blood-coagulation factor VIII, von Willebrand's (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 1

L73 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:576413 HCAPLUS
DOCUMENT NUMBER: 122:293800
TITLE: Preparing purified heparin fractions with low nitroso compound contents for use in pharmaceutical compositions
INVENTOR(S): Branellec, Jean-Francois; Espejo, Jose; Picart, Philippe
PATENT ASSIGNEE(S): Choay S.A., Fr.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623629	A1	19941109	EP 1994-400994	19940506
EP 623629	B1	19960821		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2704861	A1	19941110	FR 1993-5534	19930507
FR 2704861	B1	19950728		
CA 2122930	AA	19941108	CA 1994-2122930	19940505
AU 9461912	A1	19941110	AU 1994-61912	19940505
AU 672291	B2	19960926		
FI 9402095	A	19941108	FI 1994-2095	19940506
NO 9401686	A	19941108	NO 1994-1686	19940506
BR 9401920	A	19941129	BR 1994-1920	19940506
ZA 9403152	A	19950109	ZA 1994-3152	19940506
HU 70553	A2	19951030	HU 1994-1446	19940506
AT 141618	E	19960915	AT 1994-400994	19940506
ES 2093494	T3	19961216	ES 1994-400994	19940506
US 5599801	A	19970204	US 1994-239320	19940506
IL 109587	A1	19970415	IL 1994-109587	19940506
RU 2133253	C1	19990720	RU 1994-15595	19940506
PL 178294	B1	20000428	PL 1994-303336	19940506
CZ 287889	B6	20010314	CZ 1994-1132	19940506
CN 1096034	A	19941207	CN 1994-105382	19940507
CN 1066155	B	20010523		
TW 438812	B	20010607	TW 1994-83104157	19940507
JP 07126302	A2	19950516	JP 1994-95337	19940509

PRIORITY APPLN. INFO.: FR 1993-5534 A 19930507

AB The title fractions, with nitroso compd. content .ltoreq.500 ppb, are prepd. by **depolymn.** with HNO2. A 10.3% aq. soln. (pH 2.5) of 20 kg Na heparin was stirred with 572 g NaNO2 and sufficient HCl to maintain a pH of 2.5 until reaction was complete, adjusted to pH 10, stirred with 200 g NaBH4 for 15 h, acidified to pH 3.5-4, fractionated by pptn. with EtOH, treated with UV light (254 nm) for 9 min, purified by chromatog. on an anion exchanger, and treated with CaCl2 to give Ca heparin contg. 53 ppb nitroso compds.; vs. 3150 without UV treatment.

=> d ind

L73 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
CC 44-5 (Industrial Carbohydrates)

Section cross-reference(s): 63

ST heparin fractionated nitroso compd **removal**; UV photolysis nitroso compd heparin; pharmaceutical heparin purifn; nitrous acid **depolymn heparin**

IT Ultraviolet radiation
(nitroso compd. **removal** by, from heparin fractions)

IT **Depolymerization**
(of **heparin** by nitrous acid, purifn. in)

IT Pharmaceuticals
(prepg. purified heparin fractions with low nitroso compd. contents for use in pharmaceutical compns.)

IT Nitroso compounds
RL: REM (Removal or disposal); PROC (Process)
(**removal** of, from heparin fractions by UV light)

IT 7782-77-6, Nitrous acid
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(**depolymn.** of **heparin** in presence of, purifn. in)

IT 9041-08-1P, **Heparin sodium** salt 37270-89-6P, Heparin calcium salt
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepg. purified **heparin** fractions with low nitroso compd. contents for use in pharmaceutical compns.)

=> d ibib abs hitstr 2

L73 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:183690 HCAPLUS
DOCUMENT NUMBER: 118:183690
TITLE: Preparation of affinity-fractionated, heparin-derived oligosaccharides and their effects on selected biological activities mediated by **basic** fibroblast growth factor
AUTHOR(S): Ishihara, Masayuki; Tyrrell, David J.; Stauber, Gregory B.; Brown, Suzy; Cousens, Lawrence S.; Stack, Robert J.
CORPORATE SOURCE: Glycomed Incorp., Alameda, CA, 94501, USA
SOURCE: J. Biol. Chem. (1993), 268(7), 4675-83
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Homogeneously sized, heparin-derived oligosaccharides were prepd. from **heparin** following partial **depolymn.** with nitrous acid, redn. with **sodium** borohydride, and fractionation by gel permeation chromatog. The resulting pools of di-, tetra-, hexa-, octa-, and decasaccharides were sequentially applied to an affinity column of human recombinant **basic** fibroblast growth factor (bFGF) covalently attached to Sepharose 4B and further fractionated into subpools based on their elution from this column in response to gradients of **sodium** chloride. The homogeneously sized pools and affinity-fractionated subpools of heparin-derived oligosaccharides were quant. assessed as inhibitors or enhancers of specific bFGF-mediated biol. activities in five sep. assay systems as follows: assay 1, competition with human lymphoblastoid cells expressing syndecan (RO-12 UC cells) for binding to bFGF-coated wells; assay 2, inhibition of 125I-bFGF binding to low-affinity sites of adrenocortical endothelial (ACE) cells; assay 3, inhibition of bFGF-induced proliferation of ACE cells; assay 4, support of mitogenic activity of bFGF in a growth stimulation assay of chlorate-treated ACE cells; and assay 5, enhancement of the in vitro interaction between 125I-bFGF and the recombinant extracellular domain of FGF high-affinity receptor. Heparin-derived hexa- and octasaccharides inhibited the interaction between cell surface heparan sulfate proteoglycan and bFGF (assays 1 and 2) and bFGF-induced proliferation of ACE cells (assay 3), but they were unable to enhance the binding of bFGF to its high-affinity receptor in vitro (assay 5) or to support bFGF-induced mitogenesis in ACE cells (assay 4). These two activities required at least a decasaccharide with high affinity for bFGF.

=> d ibib abs hitstr 3

L73 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:108670 HCAPLUS
DOCUMENT NUMBER: 116:108670
TITLE: Preparation of mixed polysaccharide sulfates with low molecular weight
INVENTOR(S): Debrie, Roger
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S. A., Fr.
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4121115	A1	19920102	DE 1991-4121115	19910626
FR 2663639	A1	19911227	FR 1990-8013	19900626
FR 2663639	B1	19940318		
NL 9101049	A	19920116	NL 1991-1049	19910618
AU 9179288	A1	19920102	AU 1991-79288	19910624
AU 643531	B2	19931118		
GB 2245898	A1	19920115	GB 1991-13589	19910624
GB 2245898	B2	19931006		
IL 98604	A1	19980815	IL 1991-98604	19910624
NO 9102485	A	19911227	NO 1991-2485	19910625
DK 9101243	A	19911227	DK 1991-1243	19910625
CA 2045433	AA	19911227	CA 1991-2045433	19910625
FI 9103101	A	19911227	FI 1991-3101	19910625
SE 9101957	A	19911227	SE 1991-1957	19910625
SE 506267	C2	19971124		
HU 57796	A2	19911230	HU 1991-2122	19910625
HU 210925	B	19950928		
ZA 9104869	A	19920429	ZA 1991-4869	19910625
JP 04226101	A2	19920814	JP 1991-179030	19910625
ES 2036922	A1	19930601	ES 1991-1505	19910625
ES 2036922	B1	19940301		
CH 682236	A	19930813	CH 1991-1884	19910625
BE 1006827	A3	19950103	BE 1991-607	19910625
US 5389618	A	19950214	US 1993-92577	19930716

PRIORITY APPLN. INFO.: FR 1990-8013 19900626
US 1991-721315 19910626

AB Sulfates of polysaccharides with the **basic** structure of those in heparin and mol. wt. less than that of heparin (9-20% with mol. wt. <2000, 5-20% with mol. wt. .gtoreq.8000, polydispersity 1.3-1.6) are prepd. The sulfates are useful in preventing venous thromboses after operations. Thus, heparin benzyl ester Na salt (degree of esterification 13.3%, prepd. from heparin benzethonium salt and PhCH2Cl) was heated (10 g) in H2O with 0.9 g NaOH at 62.degree. for 1.5 h, neutralized with HCl, concd., and mixed with MeOH to give a product with wt.-av. mol. wt. 3900, polydispersity 1.39, and anticoagulant activity 22.6 IU, contg. 20% chains with mol. wt. <2000 and 5.5% with mol. wt. >8000.

IT **81209-41-8DP, Heparin** benzyl ester **sodium** salt, **depolymd.**
RL: PREP (Preparation)
(antithrombotics, prepn. and activity of)

RN 81209-41-8 HCAPLUS

CN Heparin, phenylmethyl ester, sodium salt (9CI) (CA INDEX NAME)

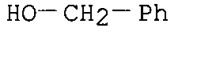
CM 1

CRN 9005-49-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 100-51-6
CMF C7 H8 O



=> d ind 3

L73 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
ICS C08L005-10; A61K031-725
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
ST benzyl ester **heparin depolymn; heparin depolymd** anticoagulant; benzethonium heparinate benzylation
IT Anticoagulants and Antithrombotics
(**depolymd. heparin**, prepn. and activity of)
IT **81209-41-8DP, Heparin** benzyl ester **sodium** salt, **depolymd.**
RL: PREP (Preparation)
(antithrombotics, prepn. and activity of)
IT 50732-58-6P, Heparin benzethonium salt
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and benzylation of)
IT 100-44-7, Benzyl chloride, reactions
RL: RCT (Reactant)
(reaction of, with heparin benzethonium salt)

=> d ibib abs hitstr 4

L73 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:538565 HCAPLUS
DOCUMENT NUMBER: 115:138565
TITLE: Supersulfated heparins with high antithrombotic activity
INVENTOR(S): Conti, Renato; Casati, Paolo; Gorini, Maria Beatrice; Maggi, Antonio
PATENT ASSIGNEE(S): Iketon Farmaceutici S.r.l., Italy
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 432537	A2	19910619	EP 1990-122309	19901122
EP 432537	A3	19911113		
EP 432537	B1	19950125		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 03210302	A2	19910913	JP 1990-315683	19901122
ES 2068969	T3	19950501	ES 1990-122309	19901122
US 5164378	A	19921117	US 1990-618051	19901126

PRIORITY APPLN. INFO.: IT 1989-22504 19891124

AB Treating heparin with oleum contg. 2-6% free sulfuric anhydride at -10 to +20.degree. gives the depolymd. title product having mol. wt. 2000-5000 and sulfation degree (s) 3.4-4.3. Thus, 50 g vacuum-dried Na heparinate was stirred with 400 mL of 4% SO3 oleum at 5.degree., after 5 min, raising gradually the temp. to 20.degree. and maintaining for 30 min, transferred to 5 L cold water and 30% NaOH soln. added to pH 5-9, and kept at 2-3.degree. overnight to give a sulfated heparin.

=> d ibib abs hitstr 5

L73 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:672 HCAPLUS
DOCUMENT NUMBER: 112:672
TITLE: Preparation of a low-molecular-weight heparin with antithrombotic activity
INVENTOR(S): Lopez Belmonte, Lorenzo
PATENT ASSIGNEE(S): Laboratorios Farmaceuticos Rovi S. A., Spain
SOURCE: Span., 5 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2003197	A6	19881016	ES 1987-20	19870105
EP 293539	A2	19881207	EP 1987-500051	19870722
EP 293539	A3	19890412		
EP 293539	B1	19940608		
R: AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE				
AT 106901	E	19940615	AT 1987-500051	19870722
PRIORITY APPLN. INFO.:			ES 1987-20	19870105
			EP 1987-500051	19870722

AB **Heparin** is **depolymd**. to a product of mol. wt. 2500-6000 by treating a quaternary ammonium salt of heparin with a quaternary ammonium **hydroxide** in a hydroxylated solvent at 10-60.degree., followed by optional treatment with NaBH4 and KMnO4. The product, isolated as the Na, Ca, or Mg salt, has long-lasting antithrombotic activity. Benzethonium heparinate was hydrolyzed with benzyltrimethylammonium **hydroxide** in CH2Cl2-MeOH at room temp.; after addn. of Triton B, the product was pptd. with 10% NaOAc in MeOH. The product had a mol. wt. of 6000, an anti-Factor Xa activity of 140 units/mg, an anticoagulant activity of 65 USP units/mg, an ED50 of 0.20 mg/kg in rats, and an LD50 of >1600 mg/kg i.v. in rats.

=> d ind 5

L73 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
CC 1-8 (Pharmacology)
Section cross-reference(s): 44
ST **heparin depolymn** antithrombotic
IT Anticoagulants and Antithrombotics
(heparin hydrolysis products)
IT Polymer degradation
(of heparin, in antithrombotic prepn.)
IT Quaternary ammonium compounds, reactions
RL: RCT (Reactant)
(heparinates, hydrolysis of, in antithrombotic prepn.)
IT 100-85-6, Benzyltrimethylammonium **hydroxide**
RL: BIOL (Biological study)
(heparin hydrolysis with, in antithrombotic prepn.)
IT 9002-05-5, Blood-coagulation factor Xa
RL: PROC (Process)
(inhibition of, by heparin hydrolysis products)

IT 9041-08-1P, Heparin **sodium** salt 37270-89-6P, Heparin calcium salt 54479-70-8P, Heparin magnesium salt
RL: SPN (Synthetic preparation); PREP (Preparation)
(low-mol.-wt., prepn. of, as antithrombotic)

IT 9005-49-6DP, Heparin, hydrolysis products 50732-58-6DP, Benzethonium heparinate, hydrolysis products
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antithrombotics)

=> d ibib abs hitstr 6

L73 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:121368 HCAPLUS
DOCUMENT NUMBER: 110:121368
TITLE: Depolymerization of natural polyanions, such as nucleic acids and glycosaminoglycans
PATENT ASSIGNEE(S): Ajorca S. A., Argent.
SOURCE: Belg., 10 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 1000118	A6	19880405	BE 1987-861	19870804
ES 2007373	A6	19890616	ES 1987-2175	19870724
CH 678326	A	19910830	CH 1987-2953	19870731
SU 1639432	A3	19910330	SU 1987-4203197	19870803
CN 87105497	A	19880413	CN 1987-105497	19870805

PRIORITY APPLN. INFO.: AR 1986-304799 19860805

AB The title process is carried out with **H2O2**, in the presence of Fe(II) salts, by a process involving formation of free radicals. Heparin Na (20 g) in 100 mL water was treated with 4 g Amberlite IR-120 (H+) followed by filtration. The filtrate (pH 4-4.5) was heated at 80.degree., with 4 mL 30% **H2O2** and 0.2 mL Fe(II) compd. soln. (1.5 g FeSO4.7H2O in 100 mL water). After 1 h the reaction was stopped with EtOH. The av. mol. wt. of the **depolymd. heparin** Na was 4.000, as compared to 12,000 for the starting product.

=> d ibib abs hitstr 7

L73 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:478204 HCAPLUS
DOCUMENT NUMBER: 107:78204
TITLE: Depolymerized hexosaminoglucan sulfates with antithrombotic, fibrinolytic, and antiinflammatory activity
INVENTOR(S): Mascellani, Giuseppe; Bianchini, Pietro
PATENT ASSIGNEE(S): Opocrin S.p.A., Italy
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8606729	A1	19861120	WO 1986-EP291	19860515
W: AU, DK, HU, JP, NO, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
DD 251355	A5	19871111	DD 1986-290192	19860513
IL 78772	A1	19910816	IL 1986-78772	19860513
AU 8659533	A1	19861204	AU 1986-59533	19860515
AU 601910	B2	19900920		
EP 221977	A1	19870520	EP 1986-903331	19860515
EP 221977	B1	19900808		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63500184	T2	19880121	JP 1986-503130	19860515
JP 2510177	B2	19960626		
HU 46028	A2	19880928	HU 1986-3344	19860515
HU 203565	B	19910828		
AT 55396	E	19900815	AT 1986-903331	19860515
ZA 8603651	A	19870128	ZA 1986-3651	19860516
CA 1283098	A1	19910416	CA 1986-509396	19860516
CN 86104301	A	19870304	CN 1986-104301	19860517
CN 1009096	B	19900808		
DK 8700157	A	19870113	DK 1987-157	19870113
DK 173804	B1	20011105		
US 4973580	A	19901127	US 1989-349706	19890510

PRIORITY APPLN. INFO.:

IT 1985-20769	A	19850517
EP 1986-903331	A	19860515
WO 1986-EP291	A	19860515
US 1987-6497	B1	19870109

AB The title polysaccharides were prepd. by a free radical-initiated **depolymn.** of natural polysaccharides, such as **heparins**, heparan sulfates, dermatan sulfates, chondroitin sulfates, and hyaluronic acid in aq. soln. at 20-70.degree. using a **peroxide** selected from the group consisting of AcOOH, 3-ClC6H4C(O)OOH, **H2O2**, cumene hydroperoxide, Na2S2O8, and BzOOH, and a catalyst selected from Cu2+, Fe2+, Cr3+ and Cr2O72-. They are useful as antithrombotic, fibrinolytic and antiinflammatory agents with poor or no anticoagulant activity. Thus, 9% aq. **H2O2** was added with stirring at 35-60.degree. in 2.5 h to a soln. of 1 kg HFA 15 raw heparin, 0.495 kg NaCl, and 1 kg AcONa in 10 L H2O contg. 0.46 g Cu(OAc)2.H2O while holding the pH at 7.5 by addn. of 1N NaOH. The mixt. was successively treated with EDTA, AcOH, and MeOH to give a ppt. which was redissolved in H2O and again treated as described above to give 845.5 g heparin with mol. wt. of

4600. This showed activated anti-factor X activity in vitro.

=> d ibib abs hitstr 1

L102 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:432654 HCAPLUS
DOCUMENT NUMBER: 133:37511
TITLE: Danaparoid sodium
AUTHOR(S): Acostamadiedo, Jose M.; Iyer, Uma G.; Owen, John
CORPORATE SOURCE: Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA
SOURCE: Expert Opinion on Pharmacotherapy (2000), 1(4), 803-814
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 53 refs. Danaparoid **sodium** (Orgaran, Organon) is a **heparinoid** glycosamino-**glycuronan** antithrombotic agent approved for the prophylaxis of post-operative deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE) in patients undergoing elective hip replacement surgery. Danaparoid is a low **mol. wt.** heparinoid consisting of a mixt. of heparan sulfate (84%), dermatan sulfate (12%) and small amts. of chondroitin sulfate (4%), whose antithrombotic activity has been well established. Its pharmacol. effect is exerted primarily by inhibiting Factors **Xa** (FXa) and **IIa** (FIIa) at a ratio greater than heparin, with a minimal effect on platelet function. Danaparoid exhibits low cross-reactivity with heparin-induced antibodies when compared with heparin or low **mol. wt.** heparins (LMWH), thereby making it an excellent choice for the management of heparin-induced thrombocytopenia (HIT). It has excellent bioavailability following s.c. injection. Danaparoid has little effect on routine coagulation tests (activated partial thromboplastin time [aPTT], prothrombin time [PT], and thrombin time [TT]). Patients with elevated serum creatinine should be monitored carefully. For its FDA approved indication (DVT prophylaxis during hip replacement surgery), its cost per day is approx. eight times more than LMWH. Even though monitoring is not routinely necessary according to the manufacturer for its approved indication, monitoring is frequently necessary when it is used in other clin. scenarios. Its higher cost than comparable therapies for DVT prophylaxis and the low availability of the FXa assay in most non-tertiary care hospitals has limited the widespread use of danaparoid. Danaparoid has been found to be effective in the treatment of HIT although this is an off label use, despite being the most frequent reason why danaparoid is used.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L102 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:975757 HCAPLUS
DOCUMENT NUMBER: 123:350100
TITLE: Accelerated Stability Studies of Heparin
AUTHOR(S): Jandik, Kenneth A.; Kruep, Dale; Cartier, Michelle; Linhardt, and Robert J.
CORPORATE SOURCE: College of Pharmacy, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: J. Pharm. Sci. (1996), 85(1), 45-51
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to extend our understanding of the stability of heparin. **Sodium heparin**, derived from porcine intestinal mucosa, was first incubated in 0.1N HCl and 0.1N NaOH at 30 and 60.degree. and sampled at times ranging from 0 to 1000 h. The absorbance spectra of the products formed under basic conditions showed an UV maxima at 232 nm assocd. with chem. catalyzed .beta.-elimination at the **uronic** acid residues. The products formed under acidic conditions showed a decreased staining intensity consistent with desulfation and a decrease in **mol. wt.** corresponding to hydrolysis of glycosidic linkages when analyzed by gradient polyacrylamide gel electrophoresis. **Heparin** samples were next prepd. in 10 mM **sodium** phosphate buffer at pH 7.0 in sealed ampules that had been flushed with nitrogen and incubated at 100.degree.. Samples taken at times ranging from 0 to 4000 h were then analyzed. Heparin was relatively stable over the first 500 h, after which it rapidly degraded. Heparin, assayed using both anti-factor **Xa** and anti-factor **IIa** amidolytic methods retained 80-90% of its activity over the first 500 h, but these activities dropped precipitously, to .apprx.6% and .apprx.0.5% of the initial activity at 1000 h and 2000 h, resp. This rapid decompn. began only after the buffering capacity of the soln. was overwhelmed by acidic degradants, which caused the pH to decrease. Decompn. processes obsd. under these conditions included the endolytic hydrolysis of glycosidic linkages and loss of sulfation, particularly N-sulfate groups, and were similar to the degrdn. processes obsd. in 0.1N HCl. This study provides initial observations on heparin degrdn. pathways. More complete, quant. studies and studies leading to the isolation and characterization of specific degradants are still required.

=> d ibib abs hitstr 1

L79 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:599979 HCAPLUS
DOCUMENT NUMBER: 125:284766
TITLE: Bioactive **heparin** surfaces from derivatization of polyacrylamide-grafted LLDPE
AUTHOR(S): Wirsen, Anders; Ohrlander, Mattias; Albertsson, Ann-Christine
CORPORATE SOURCE: Dep. of Polymer Technology, Royal Inst. of Technology, Stockholm, S-100 44, Swed.
SOURCE: Biomaterials (1996), 17(19), 1881-1889
CODEN: BIMADU; ISSN: 0142-9612
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Primary amine groups were introduced into polyacrylamide-LLDPE films, using the Hofmann degrdn. synthesis. The Hofmann degrdn. was studied at room temp. using sodium hypochlorite and sodium **hydroxide** at different concns. Diazotized **heparin** was covalently bound to the grafted LLDPE film via the primary amine groups. Surfaces were analyzed with ESCA, ATR-IR, chloride titrn. and Toluidine Blue. Evaluation of the biol. activity of the **heparinized** surfaces was made by measuring the capacity for binding antithrombin (AT) and inhibition of the activated coagulation factor XII (FXIIa). The **heparinized** surfaces were able to bind up to 3 pmol cm-2 of AT in soln. with ionic strengths of I = 0.15 and I = 0.40. No activation of the adsorbed FXII was detected.

IT **9005-49-6DP, Heparin,** reaction products with polyacrylamide-grafted polyethylene
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bioactive **heparin** surfaces from derivatization of polyacrylamide-grafted LLDPE)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9005-49-6, Heparin,** reactions
RL: RCT (Reactant)
(bioactive **heparin** surfaces from derivatization of polyacrylamide-grafted LLDPE)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 2

L79 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:379939 HCAPLUS
DOCUMENT NUMBER: 122:196881
TITLE: Degradation behavior of ionic stepwise polyaddition polymers of medical interest
AUTHOR(S): Ferruti, P.; Ranucci, E.; Bignotti, F.; Sartore, L.; Bianciardi, P.; Marchisio, M. A.
CORPORATE SOURCE: Dip. Chim. Fis. Mater., Univ. Brescia, Brescia, 25123, Italy
SOURCE: J. Biomater. Sci., Polym. Ed. (1995), 6(9), 833-44
CODEN: JBSEEA; ISSN: 0920-5063
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Degrdn. of poly(amidoamine)s (PAAs) and some other families of polymers structurally related to PAAs of medical interest are studied. PAAs are obtained by stepwise polyaddn. of primary monoamines, or bis secondary amines, to bisacrylamides. There are several other ter-amino polymers structurally related to PAAs, such poly(amido phosphine)s (PAPs), poly(ester-amine)s (PEAs), poly(ketone-amine)s (**PKAs**), poly(amidothioetheramine)s (PATAs) poly(ester-thioetheramine)s (PTEAs), and poly(sulfone thioetheramine)s (PSTAs). Most of the PAAs exhibit **heparin** complexing ability. PAAs are also being considered as sol. carriers for delivering anti-cancer drugs. Some of these polymers have been studied as antimicrobial agents. PAAs with different structures degrade at different rates under physiol. conditions. The degrdn. rate is also strongly influenced by pH. The quaternized PATAs and PTEAs are reasonably stable over a period of some days, but ultimately degrade to oligomeric products, while the quaternized PAAs do rapidly degrade.

=> d ibib abs hitstr 3

L79 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:410731 HCAPLUS
DOCUMENT NUMBER: 119:10731
TITLE: Preparation of highly-sulfated **heparins** having improved antithrombotic activity
INVENTOR(S): Nagasawa, Kinzo; Uchama, Hideki
PATENT ASSIGNEE(S): Terumo Corp, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05032703	A2	19930209	JP 1991-210096	19910726

AB The title **heparins** are prepd. by heating the solid state or dispersion in a stabilized medium of salts between **heparin** and an arom. heterocyclic **base** to effect the intramol. migration of N-sulfate groups onto OH groups, and further sulfating the sulfate-depleted amino groups, followed by depolymn. of the substrate and/or fractionation to yield the low mol. wt. fractions. A **heparin**-pyridinium salt was prepd., desiccated with P2O5, heated 90 min at 90.degree., cooled, solubilized in water, sulfated, and depolymd.
IT **9005-49-6DP, Heparin,** N-sulfated and partially depolymd.
RL: PREP (Preparation)
(antithrombotic, manuf. of)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ind 3

L79 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
ICA A61K031-725
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
ST antithrombotic sulfated **heparin** low mol wt
IT **Depolymerization**
(of **heparins** after N-sulfation, for antithrombotic agents)
IT Sulfation
(of N-position heat-induced intramol. sulfonyl-rearranged **heparin**, for antithrombotic agents)
IT Anticoagulants and Antithrombotics
(N-sulfated **heparins** for, low mol. wt.)
IT Rearrangement
(intramol., thermal, of sulfonyl groups of **heparins**, followed by N-sulfation and depolymn.)
IT **9005-49-6DP, Heparin,** N-sulfated and partially depolymd.
RL: PREP (Preparation)
(antithrombotic, manuf. of)
IT 75803-60-0

RL: RCT (Reactant)
(heating and N-sulfation of, for manuf. of antithrombotic agents)

=> d ibib abs hitstr 4

L79 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:187879 HCAPLUS
DOCUMENT NUMBER: 114:187879
TITLE: Depolymerization of quarternary salts of **heparin** for use as antithrombotics
INVENTOR(S): Lopez, Lorenzo L.
PATENT ASSIGNEE(S): Spain
SOURCE: U.S., 4 pp. Cont. of U.S. Ser. No. 212,568, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4981955	A	19910101	US 1990-485756	19900226
PRIORITY APPLN. INFO.:			US 1988-212568	19880628

AB The title process uses quaternary ammonium **hydroxides**. A mixt. of 10 g benzetonium **heparinate** (I) in 50 mL CH2Cl2 with 2 mL 40% methanolic Triton B was allowed to settle for 24 h at room temp., mixed with 2 mL Triton B soln., and, after 24 h, mixed with 50 mL 10% methanolic AcONa to give 2.9 g depolymd. I with mol. wt. 6000, optical rotation +41.degree., S content 11.5%, N content 2.1, anti-Xa activity 140, and anticoagulant activity 65.

IT **50732-58-6DP**, depolymd.
RL: PREP (Preparation)
(antithrombotic and anticoagulant, manuf. of)
RN 50732-58-6 HCAPLUS
CN Heparin, ion (neg.), N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]benzenemethanaminium (9CI) (CA INDEX NAME)

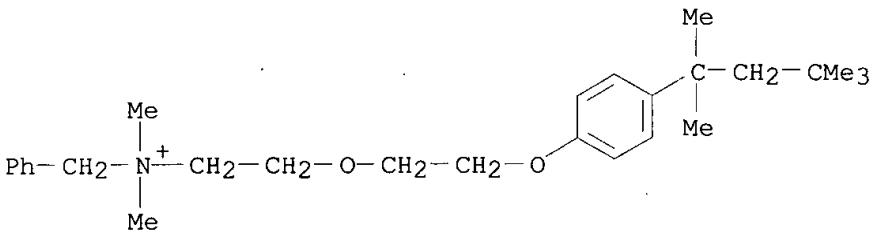
CM 1

CRN 51053-42-0
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 10172-60-8
CMF C27 H42 N O2



=> d ind 4

L79 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
ICS C07H023-00; A61K031-725; A61K031-715
NCL 536021000
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
ST anticoagulant **heparin** depolymn; antithrombotic **heparin** depolymd; benzetonium **heparinate** depolymn; quaternary ammonium **hydroxide** depolymn
IT Anticoagulants and Antithrombotics
(depolymd. **heparins** as, prepn. of)
IT Quaternary ammonium compounds, uses and miscellaneous
RL: USES (Uses)
(**heparinates**, depolymd., antithrombotic and anticoagulant, manuf. of)
IT Quaternary ammonium compounds, uses and miscellaneous
RL: USES (Uses)
(**hydroxides**, depolymn. of **heparins** in presence of)
IT **Depolymerization**
(reductive, of **heparin** quaternary ammonium salts, for antithrombotics)
IT **50732-58-6DP**, depolymd.
RL: PREP (Preparation)
(antithrombotic and anticoagulant, manuf. of)
IT 100-85-6, Triton B
RL: PROC (Process)
(depolymn. of **heparins** in presence of)

=> d ibib abs hitstr 1

L86 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:565113 HCAPLUS
DOCUMENT NUMBER: 135:147424
TITLE: Derivatives of partially desulfated glycosaminoglycans endowed with antiangiogenic activity and devoid of anticoagulating effect, and process for their preparation
INVENTOR(S): Casu, Benito; Torri, Giangiacomo; Naggi, Anna Maria; Giannini, Giuseppe; Pisano, Claudio; Penco, Sergio
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.P.A., Italy
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055221	A1	20010802	WO 2001-IT34	20010124

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2000-RM41 A 20000125
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Partially desulfated glycosaminoglycan derivs. are described, particularly heparin, and more particularly I [U = Q1-Q4 (X, X' = aldehyde, CH2D (D = OH, amino acid, peptide, carbohydrate residue, oligosaccharide residue)); R, R1 = SO3, acetyl; n, m = 1-40 (n+m = 6-40; m:n ratio = 10:2-1:1; zig-zag-like symbol indicates that the units marked m and n are statistically distributed along polysaccharide chain and not necessarily in sequence)]. The glycosaminoglycan derivs. have antiangiogenic activity and are devoid of anticoagulant activity. A process for prepg. the derivs. of the invention is also provided.

IT **9005-49-6**, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); RACT (Reactant or reagent)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

=> d ind 1

L86 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
IC C08B037-10; A61K031-726; A61K031-727; A61K031-715
CC 1-8 (Pharmacology)
Section cross-reference(s): 33
ST angiogenesis inhibitor desulfated glycosaminoglycan prepn; heparin desulfated prepn angiogenesis inhibitor
IT **Hydrolysis**
(acid; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Artery
(angioplasty, restenosis after; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Artery
(coronary, bypass surgery, restenosis after; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Artery, disease
(coronary, restenosis; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Eye, disease
(diabetic retinopathy; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Functional groups
(diol; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Blood vessel
(endothelium; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT **Hydrolysis**
(enzymic; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Antitumor agents
(metastasis; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Angiogenesis inhibitors
Antitumor agents
Cell adhesion
Drug delivery systems
Epoxy group
Formyl group
Oxidation
Psoriasis
Reduction
Ring opening
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)
IT Glycosaminoglycans, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Uronic acids
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Oligosaccharides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Functional groups
(primary alc.; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Proliferation inhibition
(proliferation inhibitors; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Artery, disease
(restenosis; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Eye, disease
(retrolental fibroplasia; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Sulfation
(retrosulfation; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Oligosaccharides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(tetrasaccharides, and octasaccharides; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT Fibroblast growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type 1; partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 9041-08-1, **Sodium heparin** 352437-72-0 352437-73-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 9025-39-2, Heparinase 9055-04-3, Lyase 52227-76-6, Heparitinase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT **9005-49-6**, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); RACT (Reactant or reagent)

(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 53260-52-9P, Desulfated heparin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 64859-64-9, N-Acetyl-N-desulfo heparin 196887-68-0, 2-O-Desulfated heparin 352437-74-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 685-73-4, Galacturonic acid 3402-98-0, Iduronic acid 3402-98-0D, Iduronic acid, unsatd. derivs. 4607-22-1, N-Sulfoglucosamine
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

IT 7790-28-5, Sodium periodate
RL: RCT (Reactant); RACT (Reactant or reagent)
(partially desulfated glycosaminoglycan derivs. with antiangiogenic activity and devoid of anticoagulating effect, and prepn. process)

=> d ibib abs hitstr 2

L86 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:395643 HCAPLUS
DOCUMENT NUMBER: 133:26855
TITLE: Modified low-molecular-weight heparin that inhibits clot-associated coagulation factors
INVENTOR(S): Weitz, Jeffrey I.; Hirsh, Jack
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6075013	A	20000613	US 1998-92325	19980605

PRIORITY APPLN. INFO.: US 1998-72098P P 19980606

AB Compns. and methods are provided for the treatment of cardiovascular diseases. More particularly, the invention relates to modifying thrombus formation by administering an agent which, inter alia, is capable of (1) inactivating fluid-phase thrombin and thrombin which is bound either to fibrin in a clot or to some other surface by catalyzing antithrombin; and (2) inhibiting thrombin generation by catalyzing factor Xa inactivation by antithrombin III (ATIII). The compns. and methods of the invention are particularly useful for preventing thrombosis in the circuit of cardiac bypass app. and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, e.g. unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.

IT **9005-49-6P**, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 2

L86 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
IC ICM A61K031-725
NCL 514056000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
ST modified low mol wt heparin coagulation factor inhibition; antithrombotic modified low mol wt heparin

IT Thrombosis
(arterial; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Artery
(atherectomy, increased risk for thrombus in; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT **Hydrolysis**
(base, heparin limited periodate oxidn./**hydrolysis**; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Heart
(cardiac catheterization, increased risk for thrombus in; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Medical goods
(catheters, catheterization, increased risk for thrombus in; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Thrombosis
(coronary arterial; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Artery, disease
Artery, disease
(coronary, thrombosis; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Artery, disease
(coronary, thrombus due to; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Lung, disease
(embolism; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(exosite 2; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Oxidation
(heparin limited periodate oxidn./**hydrolysis**; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Cardiopulmonary bypass
(increased risk for thrombus in; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Drug delivery systems
(injections; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Allosterism
Anticoagulants
Blood coagulation
Drug delivery systems
Molecular association

(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Fibrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Heart
(surgery, increased risk for thrombus in; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Atherosclerosis
(thrombus due to; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Thrombosis
(venous; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 7790-28-5, **Sodium** periodate
RL: RCT (Reactant); RACT (Reactant or reagent)
(**heparin** limited periodate oxidn./**hydrolysis**; modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 8001-27-2, Hirudin 78768-79-3, Prothrombin fragment 2 121822-23-9, Hirugen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT **9005-49-6P**, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 9000-94-6, Antithrombin 9002-04-4, Blood coagulation factor IIa 9002-05-5, Blood coagulation factor Xa
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(modified low-mol.-wt. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

=> d ibib abs hitstr 3

L86 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:160928 HCAPLUS
DOCUMENT NUMBER: 112:160928
TITLE: Heparin derivatives for pharmaceuticals and process for their preparation
INVENTOR(S): Piani, Silvano; Tamagnone, Gianfranco; Alpino, Raul Roberto; Milani, Maria Rita; Fantuz, Marinella
PATENT ASSIGNEE(S): Alfa Wassermann S.p.A., Italy
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 347588	A1	19891227	EP 1989-109030	19890519
EP 347588	B1	19940727		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2012748	T3	19941016	ES 1989-109030	19890519
ZA 8903882	A	19900228	ZA 1989-3882	19890523
AU 8935128	A1	19891214	AU 1989-35128	19890524
AU 611028	B2	19910530		
US 5010063	A	19910423	US 1989-357548	19890526
IL 90411	A1	19930513	IL 1989-90411	19890526
DK 8902850	A	19891211	DK 1989-2850	19890609
DK 173818	B1	20011119		
FI 8902850	A	19891211	FI 1989-2850	19890609
FI 94534	B	19950615		
FI 94534	C	19950925		
NO 8902366	A	19891211	NO 1989-2366	19890609
NO 174259	B	19931227		
NO 174259	C	19940406		
JP 02064102	A2	19900305	JP 1989-148211	19890609
JP 07039442	B4	19950501		
CA 1309402	A1	19921027	CA 1989-602338	19890609

PRIORITY APPLN. INFO.: IT 1988-3504 A 19880610

AB Title derivs., having antithrombotic activity and reduced hemorrhagic and anticoagulant effects, are prepd. by treating heparins in a basic medium, optionally in the presence of alkali metal salts and a reducing agent. The derivs. exhibit C-13 NMR shifts at 53 and 54 ppm and a sp. rotation ([.alpha.]D20) of +50.degree. to +90.degree.. A purified heparin (S 10.56%, sulfate-COOH ratio 2.20, [.alpha.]D20 +47.degree.) (1.8 g) was heated in 45 mL H2O contg. NaOH 0.4, NaOAc 2.38 and NaBH4 0.01 g at 60.degree. for 3.5 h to give a deriv.

IT **9005-49-6**, Heparin, reactions
RL: **RCT (Reactant)**
(modification of, for antithrombotic agents)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ind 3

L86 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C08B037-10
ICS A61K031-725
CC 44-5 (Industrial Carbohydrates)
Section cross-reference(s): 63
ST antithrombotic heparin deriv prepn; alkali **hydrolysis** heparin deriv antithrombotic; redn agent heparin deriv antithrombotic
IT Reducing agents
Bases, biological studies
Chlorides, biological studies
Salts, biological studies
Sulfates, biological studies
RL: BIOL (Biological study)
(heparin treatment by, in manuf. of antithrombotic agents)
IT 10043-52-4, Calcium chloride, biological studies 10361-37-2, Barium chloride, biological studies 16940-66-2, **Sodium** borohydride (NaBH4) 62-54-4, Calcium acetate 127-08-2, Potassium acetate 127-09-3, **Sodium** acetate 142-72-3, Magnesium acetate 543-80-6, Barium acetate 1310-73-2, **Sodium** hydroxide, biological studies 7447-40-7, Potassium chloride, biological studies 7487-88-9, Magnesium sulfate, biological studies 7647-14-5, **Sodium** chloride, biological studies 7757-82-6, **Sodium** sulfate, biological studies 7778-80-5, Potassium sulfate, biological studies 7786-30-3, Magnesium chloride, biological studies
RL: BIOL (Biological study)
(**heparin** treatment by, in manuf. of antithrombotic agents)
IT 9041-08-1, **Sodium heparin**
RL: PROC (Process)
(modification of, for antithrombotic agents)
IT **9005-49-6**, Heparin, reactions
RL: **RCT (Reactant)**
(modification of, for antithrombotic agents)
IT 9005-49-6DP, Heparin, **hydrolyzed**, reduced 9041-08-1DP, **Sodium heparin**, **hydrolyzed**, reduced
RL: PREP (Preparation)
(prepn. of, as antithrombotic agents)

Priority 7/21/2000.

KRISHNAN 09/909,797

=> d ibib abs hitstr 1

L103 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:199745 HCAPLUS
DOCUMENT NUMBER: 136:318708
TITLE: Reviparin **sodium** - a new low **molecular weight heparin**
AUTHOR(S): Breddin, Hans Klaus
CORPORATE SOURCE: International Institute of Thrombosis and Vascular Diseases e. V., Frankfurt/Main, Germany
SOURCE: Expert Opinion on Pharmacotherapy (2002), 3(2), 173-182
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Reviparin **sodium** (Clivarine, Knoll AG) is a low **mol. wt. heparin** (LMWH) with a mean peak **mol. wt.** of 3900 Da. It is characterized by a narrow **mol. wt.** distribution profile, with an anti-factor **Xa** (**anti-Xa**):anti-factor **IIa** (**anti-IIa**) ratio of .gtoreq. 3.6. In healthy human volunteers, plasma **anti-Xa** activity was up to five times higher and lasted three times longer with reviparin compared with unfractionated heparin (UFH). Unlike UFH, reviparin has negligible effects on global clotting tests. Reviparin has been shown to be as effective as UFH in different prophylactic indications and causes fewer injection-site hematomas. At a daily dose of 1750 IU **anti-Xa** it was as effective as UFH in preventing deep vein thrombosis (DVT) in moderate risk surgery (general and abdominal) and significantly reduced DVT in patients with brace immobilization of the legs. At a daily dose of 4200 IU **anti-Xa** reviparin was as effective as UFH or enoxaparin in preventing DVT in high risk orthopedic surgery and as effective as UFH in prevention of DVT and/or pulmonary embolism (PE) and/or mortality in high risk orthopedic surgery. In patients with acute venous thromboembolism (VTE), reviparin was more effective than UFH in thrombus redn. and at least as effective as UFH in the prevention of clin. recurrence of DVT and/or PE. The use of reviparin is assocd. with a similar or lower incidence of bleeding complications than UFH.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L103 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:715791 HCAPLUS
DOCUMENT NUMBER: 136:379763
TITLE: Pharmacodynamics of intravenous and subcutaneous tinzaparin and heparin in healthy volunteers
AUTHOR(S): Fossler, Michael J.; Barrett, Jeffrey S.; Hainer, James W.; Riddle, J. G.; Ostergaard, Per; Van Der Elst, Eric; Sprogel, Per
CORPORATE SOURCE: Clinical Pharmacokinetics, DuPont Pharmaceuticals, Wilmington, DE, USA
SOURCE: American Journal of Health-System Pharmacy (2001), 58(17), 1614-1621
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacodynamics of i.v. and s.c. tinzaparin **sodium** compared with **heparin** in healthy volunteers were studied. A randomized, open-label, five-treatment, five-period-crossover study with a Latin square design was performed in 30 healthy men to est. tinzaparin pharmacodynamics (**anti-Xa** and **anti-IIa** activities) after single-dose i.v. and s.c. administration, to evaluate abs. bioavailability, to det. the effect of a preservative (benzyl alc.), to evaluate the dose-activity relationship, and to compare tinzaparin with unfractionated heparin. Treatments were (1) heparin 5,000 units s.c., (2) tinzaparin 4,500 **anti-Xa** IU without preservative s.c., (3) tinzaparin 4,500 **anti-Xa** IU without preservative i.v., (4) tinzaparin 12,250 **anti-Xa** IU with preservative s.c., and (5) tinzaparin 4,500 **anti-Xa** IU with preservative s.c. Blood samples for the measurement of **anti-Xa** and **anti-IIa** activities were drawn over 24 h. **Anti-Xa** and **anti-IIa** activities were detd. by chromogenic methods; data were analyzed by using a noncompartmental approach. The clearance of tinzaparin based on **anti-Xa** activity ranged from 1.14 to 2.04 L/h. The vol. of distribution was 3.1-5.0 L, suggesting that the mol. entities responsible for **anti-Xa** and **anti-IIa** activities are confined to the intravascular space. Mean peak **anti-Xa** activity occurred three to four hours after s.c. injection, independent of the dose. The mean half-life of **anti-Xa** activity after s.c. injection ranged from 3.41 to 4.13 h and was independent of the dose. The mean abs. bioavailability of s.c. tinzaparin was 86.7%. Intersubject pharmacodynamic variability was low for tinzaparin compared with heparin. Benzyl alc. did not affect tinzaparin pharmacodynamics. A clear dose-activity relationship was seen for the two fixed doses of tinzaparin (12,250 and 4,500 IU). Single doses of tinzaparin were safe and well tolerated after administration by either route. The **anti-Xa** profile of tinzaparin supports the pharmacodynamic superiority of low-**mol.**-**wt.** heparins over std. i.v. heparin administration. This pharmacodynamic study in healthy volunteers indicates that s.c. tinzaparin sodium was well absorbed; the presence of a preservative, benzyl alc., did not affect the activity of tinzaparin; and tinzaparin activity is dose-related.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 3

L103 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:606695 HCAPLUS
DOCUMENT NUMBER: 135:326881
TITLE: Reviparin: A review of its efficacy in the prevention and treatment of venous thromboembolism
AUTHOR(S): Wellington, Keri; McClellan, Karen; Jarvis, Blair
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: Drugs (2001), 61(8), 1185-1209
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Reviparin (reviparin **sodium**) is a low **mol. wt. heparin** (LMWH) that catalyzes the inactivation of factors **Xa** and **IIa** by binding to antithrombin, which ultimately leads to the inhibition of the clotting cascade. It is administered s.c. Reviparin 7000 to 12,600 anti-XaIU/day was found to be as effective as i.v. unfractionated heparin in preventing the clin. recurrence of acute deep vein thrombosis (DVT) and/or pulmonary embolism in 1 large randomized, multicenter trial (COLUMBUS) and was significantly more effective than i.v. unfractionated heparin in the prevention of recurrent venous thromboembolism in another large randomized, multicenter trial (CORTES). Reviparin has also been compared with unfractionated heparin in children with established DVT. However, the trial was under-powered and no conclusion could be made regarding comparative efficacy. As prophylaxis, reviparin 1750 anti-XaIU once daily was as effective as unfractionated **heparin** 5000 IU twice daily in 1311 patients undergoing abdominal surgery and, in a once daily dosage of 4200 anti-XaIU, was as effective as s.c. enoxaparin **sodium** 40 mg/day or acenocoumarol in patients undergoing hip replacement surgery. Reviparin 1750 anti-XaIU also effectively prevented DVT, compared with no treatment, in patients undergoing knee arthroscopy. It was also more effective than placebo in patients with brace immobilization of the lower extremity. Reviparin was compared with "std. care" in children with central venous lines. However, the trial was too small to make conclusions regarding its efficacy. Comparative data indicate that reviparin is at least as well tolerated as **heparin** and enoxaparin **sodium**. However, in a large (n = 1279) trial there were significantly fewer major bleeding episodes in patients receiving reviparin than in patients given the oral anticoagulant acenocoumarol. The most commonly reported adverse events in therapeutic trials have been intraoperative blood loss and postoperative bleeding complications such as wound hematoma, bruising and injection site hemorrhage. Reviparin was also well tolerated in 2 studies in children aged .ltoreq.16 yr. Reviparin has shown efficacy in the treatment of established DVT and in the prevention of postoperative DVT after moderate and high risk surgery and was as effective as enoxaparin sodium or acenocoumarol in patients undergoing hip replacement surgery. As an effective and well tolerated antithrombotic agent, reviparin is likely to assume a significant role in the treatment and prevention of DVT, as it appears to have a preferable tolerability profile to s.c. heparin after moderate risk surgery and is at least as effective as i.v. heparin in the treatment of established DVT.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 4

L103 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:181817 HCAPLUS
DOCUMENT NUMBER: 134:361172
TITLE: Anticoagulant Pharmacodynamics of Tinzaparin Following 175 IU/kg Subcutaneous Administration to Healthy Volunteers
AUTHOR(S): Barrett, J. S.; Hainer, J. W.; Kornhauser, D. M.; Gaskill, J. L.; Hua, T. A.; Sprogel, P.; Johansen, K.; van Lier, J. J.; Knebel, W.; Pieniaszek, H. J.
CORPORATE SOURCE: DuPont Pharmaceuticals, Wilmington, Newark, DE, 19714, USA
SOURCE: Thrombosis Research (2001), 101(4), 243-254 adonis ? X
CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tinzaparin, a **sodium** salt of a low-**mol.-wt.** **heparin** (LMWH) produced via **heparinase** digestion, is used for the treatment of deep vein thrombosis (DVT) and pulmonary embolism in conjunction with warfarin for the prevention of DVT in patients undergoing hip or knee replacement surgery, and as an anticoagulant in hemodialysis circuits. Its av. **mol. wt**. ranges between 5500 and 7500 daltons (Da); the percentage of chains with **mol. wt.** lower than 2000 Da is not more than 10% in the marketed tinzaparin formulation. While this fraction is generally considered pharmacol. inactive, this has never been evaluated in vivo. The importance of the <2000 Da fraction on the anticoagulant pharmacodynamics of tinzaparin assessed by **anti-Xa** and **anti-IIa** activity was studied in a two-way crossover trial. In this trial, 30 healthy volunteers received a single 175 IU/kg s.c. administration of tinzaparin contg. approx. 3.5% of the <2000 Da fraction and a tinzaparin-like LMWH contg. 18.3% of the <2000 Da fraction. The **anti-Xa/anti-IIa** ratios of the drug substances were comparable at 1.5 and 1.7 for tinzaparin and the tinzaparin-like LMWH, resp. Both formulations were safe and well tolerated. Mean max. plasma **anti-Xa** activity (Amax) was approx. 0.818 IU/mL at 4 h following tinzaparin injection. Mean max. plasma **anti-IIa** activity was 0.308 IU/mL at 5 h postdose. Intersubject variation was lower (<18% for both **anti-Xa** and **anti-IIa** metrics) than in previous fixed-dose administration studies. There was no correlation between **anti-Xa** or **anti-IIa** AUC or Amax and bodyweight in the present study supporting the wt.-adjusted dosing regimen. Individual **anti-Xa** and **anti-IIa** profiles following the single 175 IU/kg s.c. administration of the tinzaparin-like LMWH were similar to that obtained with tinzaparin. Based on av. equivalence criteria, the two LMWH prepns. were detd. to be bioequivalent using either **anti-Xa** or **anti-IIa** activity as biomarkers. The calcd. intrasubject variabilities were low (<14% for **anti-Xa** activity and <18% for **anti-IIa** activity) yielding little evidence for a significant Subject.times.Formulation interaction. In summary, **anti-Xa** and **anti-IIa** activity following a single s.c. administration of tinzaparin 175 IU/kg to healthy volunteers yielded activity consistent with targeted therapeutic levels derived from previous trials in adult DVT patients. Wt.-based dosing for the treatment of DVT appears rational based on the redn. in **anti**

-Xa and **anti-IIa** variability consistent with the recommendation derived from earlier fixed-dose pharmacokinetic studies. Furthermore, differences in the percentage of mols. in the <2000 Da **mol. wt.** fraction of tinzaparin do not translate into differences in **anti-Xa** and **anti-IIa** activity in vivo.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 5

L103 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:62347 HCAPLUS
DOCUMENT NUMBER: 134:120946
TITLE: Compositions comprising very low-**molecular weight** heparin
INVENTOR(S): Mardiguian, Jean
PATENT ASSIGNEE(S): Laboratorios Farmaceuticos Rovi, S.A., Spain
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1070503	A1	20010124	EP 1999-500184	19991013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ES 2161615	A1	20011201	ES 1999-1671	19990723
BR 9905820	A	20010313	BR 1999-5820	19991028
US 6384021	B1	20020507	US 1999-433409	19991103

PRIORITY APPLN. INFO.: ES 1999-1671 A 19990723
OTHER SOURCE(S): MARPAT 134:120946

AB The invention provides a compns. of heparins of very low -**mol. wt.** having specified formula. Such compns. of heparin are composed of mixts. of oligosaccharides or fragments of heparin and are characterized by having anti-**Xa** activity and anti-factor **IIa** activity and because they can be used as antithrombotic medicaments.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 6

L103 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:31543 HCAPLUS
DOCUMENT NUMBER: 134:105837
TITLE: Medium **molecular-weight** heparin compositions that inhibit clot associated coagulation factors for treatment of cardiovascular diseases
INVENTOR(S): Weitz, Jeffrey I.; Hirsh, Jack
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development, Inc., Can.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002443	A1	20010111	WO 2000-CA774	20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000012202	A	20020402	BR 2000-12202	20000629
EP 1192187	A1	20020403	EP 2000-941847	20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-141865P P 19990630
US 1999-154744P P 19990917
WO 2000-CA774 W 20000629

AB The present invention relates to modifying thrombus formation and growth by administering a medium **mol. wt.** heparin (MMWH) compn. that, inter alia, is capable of (1) inactivating fluid-phase thrombin as well as thrombin which is bound either to fibrin in a clot or to some other surface by catalyzing antithrombin; and (2) inhibiting thrombin generation by catalyzing factor **Xa** inactivation by antithrombin III (ATIII). In addn., the present invention provides methods and compns. useful for treating cardiovascular disease. The MMWH compns. have an antifactor **IIa** activity of .apprx.40-100 U/mg and an antifactor **Xa** activity of .apprx.90-150 U/mg.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 7

L103 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:709218 HCAPLUS
DOCUMENT NUMBER: 134:231459
TITLE: Comparative pharmacokinetics of LMWHs
AUTHOR(S): Samama, Meyer M.; Gerotziafas, Grigoris T.
CORPORATE SOURCE: Service d'Hematologie Biologique, Hopital Hotel-Dieu de Paris, Paris, 75181/04, Fr.
SOURCE: Seminars in Thrombosis and Hemostasis (2000), 26(Suppl. 1), 31-38
CODEN: STHMBV; ISSN: 0094-6176
PUBLISHER: Thieme Medical Publishers, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A variety of pharmaceutical prepns. of low-**mol.-wt.** heparins (LMWHs) are available. They belong to the same family of compds.-ie, heparin derivs. with a narrow distribution of mean **mol. wts.** (**MWs**). LMWHs have different methods of prepn., which result in variations in mean **MW**, distribution of **MW**, and pharmacokinetic (PK) and pharmacodynamic (PD) profiles. The mean **MW** of these compds. ranges from 3600 to 6500 daltons. The ratio of **anti-Xa** (aXa) and **anti-IIa** (aIIa) activities of the different LMWHs ranges from 1.5 to > 10. After s.c. (SC) injection of a prophylactic or therapeutic dose, the peak values for plasma aXa or aIIa activity may vary twofold to threefold because of differences in bioavailability, plasma clearance (Clplasma), and half-life (t1/2). The injection of equiv. amts. of product, based on aXa and aIIa IU (IU), may result in different areas under the curve for the resp. activities. Although tinzaparin has a high aIIa specific activity per mg (and consequently, a low aXa/aIIa ratio), SC injection of 40 mg of enoxaparin (4000 aXa IU) results in a higher aXa peak value in patients with total hip replacement than 4500 aXa IU of tinzaparin. Differences in aIIa and aXa peak activities are more striking when high doses of LMWHs are used. The activated partial thromboplastin time (aPTT) can be significantly prolonged, an effect that is related to aIIa and aXa activity. The vol. of distribution of LMWHs is of the same order of magnitude as that of the plasma vol. The mean retention time of aXa activity varies from 5.2 (dalteparin) to .apprx.7 h (enoxaparin, nadroparin). Bioavailability of prophylactic doses of LMWHs ranges from 86% (dalteparin) to 98% (enoxaparin, nadroparin). PK parameters appear to be minimally affected by a patient's age. The Clplasma is different for each LMWH: 16 mL/min enoxaparin, 21 mL/min nadroparin, 33 mL/min dalteparin, 19 mL/min reviparin, and 22 mL/min tinzaparin. Accumulation of product has been obsd. for almost all LMWHs in patients with renal insufficiency. LMWHs are effective and safe for treatment or prophylaxis of venous thromboembolism during pregnancy, because they do not cross the placenta. No data are available regarding the passage of LMWHs into the milk in lactating women. Although LMWHs are also effective in prevention and treatment of thromboembolic disease in children, optimal use of these agents in pediatric patients has not been detd. In summary, the PD and PK of LMWHs have been well documented and have demonstrated that LMWHs have a more predictable response, a greater bioavailability, and a longer aXa t1/2 than unfractionated heparin. However, their distribution of **MW** affects their physicochem. and biol. properties, as well as PK characteristics. The concept of aXa/aIIa ratio (detd. in vitro) does not account for the differing PK of aXa and aIIa activity in circulating blood.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 8

L103 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:395643 HCAPLUS
DOCUMENT NUMBER: 133:26855
TITLE: Modified low-**molecular-weight** heparin that inhibits clot-associated coagulation factors
INVENTOR(S): Weitz, Jeffrey I.; Hirsh, Jack
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6075013	A	20000613	US 1998-92325	19980605

PRIORITY APPLN. INFO.: US 1998-72098P P 19980606

AB Compns. and methods are provided for the treatment of cardiovascular diseases. More particularly, the invention relates to modifying thrombus formation by administering an agent which, inter alia, is capable of (1) inactivating fluid-phase thrombin and thrombin which is bound either to fibrin in a clot or to some other surface by catalyzing antithrombin; and (2) inhibiting thrombin generation by catalyzing factor **Xa** inactivation by antithrombin III (ATIII). The compns. and methods of the invention are particularly useful for preventing thrombosis in the circuit of cardiac bypass app. and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, e.g. unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 8

L103 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
IC ICM A61K031-725
NCL 514056000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
ST modified low **mol wt** heparin coagulation factor inhibition; antithrombotic modified low **mol wt** heparin
IT Thrombosis
(arterial; modified low-**mol**.-**wt**. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Artery
(atherectomy, increased risk for thrombus in; modified low-**mol**.-**wt**. heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)
IT Hydrolysis
(base, heparin limited periodate oxidn./hydrolysis; modified low-**mol**.-**wt**. heparin for inhibition of clot-assocd.

coagulation factors and prevention and treatment of thrombotic conditions)

IT Heart
(cardiac catheterization, increased risk for thrombus in; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Medical goods
(catheters, catheterization, increased risk for thrombus in; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Thrombosis
(coronary arterial; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Artery, disease
Artery, disease
(coronary, thrombosis; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Artery, disease
(coronary, thrombus due to; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Lung, disease
(embolism; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(exosite 2; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Oxidation
(heparin limited periodate oxidn./hydrolysis; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Cardiopulmonary bypass
(increased risk for thrombus in; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Drug delivery systems
(injections; modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Allosterism
Anticoagulants
Blood coagulation
Drug delivery systems
Molecular association
(modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Fibrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(modified low-**mol.-wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of

thrombotic conditions)

IT Heart
(surgery, increased risk for thrombus in; modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Atherosclerosis
(thrombus due to; modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT Thrombosis
(venous; modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 7790-28-5, **Sodium** periodate
RL: RCT (Reactant); RACT (Reactant or reagent)
(**heparin** limited periodate oxidn./hydrolysis; modified low-**mol.**-**wt.** **heparin** for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 8001-27-2, Hirudin 78768-79-3, Prothrombin fragment 2 121822-23-9, Hirugen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 9005-49-6P, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

IT 9000-94-6, Antithrombin 9002-04-4, Blood coagulation factor **IIa** 9002-05-5, Blood coagulation factor **Xa**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(modified low-**mol.**-**wt.** heparin for inhibition of clot-assocd. coagulation factors and prevention and treatment of thrombotic conditions)

=> d ibib abs hitstr 9

L103 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:528171 HCAPLUS
TITLE: Absolute and comparative subcutaneous bioavailability of ardeparin **sodium**, a low **molecular weight heparin**
AUTHOR(S): Troy, Steven; Fruncillo, Richard; Ozawa, Tsunenori; Mammen, Eberhard; Holloway, Scott; Chiang, Soong
CORPORATE SOURCE: Wyeth-Ayerst Research, Philadelphia, PA, 19101, USA
SOURCE: Thromb. Haemostasis (1997), 78(2), 871-875
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: Schattauer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ardeparin **sodium** (Normiflo, Wyeth-Ayerst) is a low **mol. wt. heparin** undergoing clin. evaluation as an antithrombotic agent. The objective of this study was to evaluate the abs. and comparative bioavailability of ardeparin following s.c. administration of three different formulations [two formulations of ardeparin at 10,000 anti-factor **Xa** (aXa) U/mL, but with different preservatives, and a 20,000 aXa U/mL formulation]. The study was conducted using a randomized 4-period crossover design (three s.c. treatments and one i.v. treatment) in 24 healthy subjects, and the pharmacokinetics of ardeparin were characterized by plasma anti-factor **IIa** (aIIa) and anti-factor **Xa** (aXa) activities. The mean abs. bioavailability of ardeparin based on aIIa activity ranged from 62% to 64% and the mean abs. bioavailability based on aXa activity ranged from 88% to 97%. Based on bioequivalence testing criteria, the three ardeparin formulations were bioequivalent.

=> d ibib abs hitstr 10

L103 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:360010 HCAPLUS
DOCUMENT NUMBER: 122:151072
TITLE: Protamine neutralization of intravenous and subcutaneous low-**molecular-weight** heparin (tinzaparin, Logiparin). An experimental investigation in healthy volunteers
AUTHOR(S): Holst, J.; Lindblad, B.; Bergqvist, D.; Garre, K.; Nielsen, H.; Hedner, U.; Ostergaard, P. B.
CORPORATE SOURCE: Malmo General Hospital, University Lund, Malmoe, Swed.
SOURCE: Blood Coagulation Fibrinolysis (1994), 5(5), 795-803
CODEN: BLFIE7; ISSN: 0957-5235
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the present study was to investigate whether tinzaparin **sodium** (a low-**mol.-wt. heparin** (LMWH)) was fully and permanently neutralized in vivo in man by protamine sulfate (PS) after i.v. or s.c. injection. Fifty healthy adults equally divided in five age- and sex-matched groups were included. The groups received 50 IU unfractionated heparin (UH)/kg body wt. (b.w.) i.v., 50 anti-factor **Xa** (**anti-Xa**) IU tinzaparin/kg b.w. i.v., 75 **anti-Xa** IU tinzaparin/kg b.w. s.c., 175 **anti-Xa** IU tinzaparin/kg b.w. s.c., or 1 mL of saline s.c. PS was given as a 10 min infusion in a dose of 1 mg/100 IU of heparin in the four first groups while 0.5 mg PS/kg b.w. was given in the placebo group. In the i.v. groups PS was administered 45 min after the heparin injection, and in the s.c. groups 180 min post-heparin injection. In the UH group PS fully and permanently neutralized all three activities. In the i.v. tinzaparin group PS reversed 80% of the **anti-Xa** activity, while the **anti-IIa** and aPTT activities were fully reversed. A slight, but statistically significant, increase in **anti-Xa** and **anti-IIa** activities were seen following i.v. tinzaparin. In the s.c. groups 60-65% of the obsd. peak **anti-Xa** activity was neutralized, **anti-IIa** was almost completely reversed, and aPTT returned nearly to baseline values. A gradual return of the **anti-Xa** activity (65-75%), **anti-IIa** activity (55%) and aPTT activity (35-45%) was seen in the s.c. groups 3 h after reversal compared with the obsd. peak values. A continuous absorption of tinzaparin from the s.c. depot is presumably the cause of the returned activity. PS caused an 8-27% transient drop in the platelet count in all groups. This study confirms that the **anti-Xa** activity following i.v. and s.c. administration of tinzaparin (a LMWH) is only partially neutralizable by protamine. This is not due to insufficient dosages of the antidote, as an excess of protamine could be demonstrated ex vivo immediately after the protamine infusion. The present results suggest that protamine neutralization of tinzaparin given s.c. should be obtained with intermittent injections or continuous infusion.

=> d ibib abs hitstr 11

L103 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:45510 HCAPLUS
DOCUMENT NUMBER: 120:45510
TITLE: Action and characteristics of parnaparin sodium as an antithrombin III cofactor
AUTHOR(S): Sugiyama, Takayuki; Itoh, Mari; Okitsu, Misako; Natsuga, Tohru; Tomita, Takako
CORPORATE SOURCE: Res. Dep., Shimizu Pharm. Co., Ltd., Shimizu, 424, Japan
SOURCE: Iyakuhin Kenkyu (1993), 24(10), 1061-9
CODEN: IYKEDH; ISSN: 0287-0894
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Parnaparin **sodium** is a low-**mol. wt.** **heparin** coded LHG. The authors investigated the mechanism of action of LHG as an antithrombin III (ATIII) cofactor. From the standpoint of **mol. wt.**, no fractions with **mol. wts.** below 1500, which were incapable of serving as ATIII cofactor, were detected in LHG or unfractionated heparin (Heparin). However, 79% of LHG consisted of mols. whose **mol. wt.** was below 5400, which were incapable of expressing any antithrombin activity (**anti-IIa** activity). The **mol. wt.** of Heparin was mostly in the range above 5400. Using changes in intrinsic fluorescence as an index of binding, the ATIII-binding affinity of LHHG was less than that of Heparin, suggesting that LHG includes more fractions with low ATIII binding capacity. Moreover, there was less direct binding of **IIa**, which is an important factor for the expression of **anti-IIa** activity, by LHG than by Heparin. LHG displayed the same degree of enhancing activity on **Xa**-ATIII complex formation, measured by SDS-PAGE and sandwich ELISA, as Heparin with identical **anti-Xa** activity. On the other hand, results were obtained indicating that LHG has weaker enhancing activity on the formation of **IIa**-ATIII complex than Heparin, and that, based on measurement of formation of **Xa**-ATIII and **IIa**-ATIII complexes, LHG has a higher **anti-Xa** activity/**anti-IIa** activity ratio than Heparin.

=> d ibib abs hitstr 12

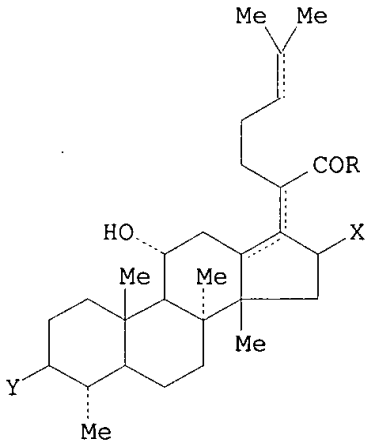
L103 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:508952 HCAPLUS
DOCUMENT NUMBER: 113:108952
TITLE: Anticoagulant and antithrombotic effects of chemically modified heparins and pentosanpolysulfate
AUTHOR(S): Krupinski, K.; Breddin, H. K.; Casu, B.
CORPORATE SOURCE: Dep. Haematol., Med. Sch., Bialystok, Pol.
SOURCE: Haemostasis (1990), 20(2), 81-92
CODEN: HMTSB7; ISSN: 0301-0147
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pig mucosal **heparin** (GAG 98), in which the binding site for antithrombin had been inactivated by periodate oxidn. (GAG 262), a supersulfated low-**mol.-wt. heparin** (GAG 869), a low-**mol.-wt. heparin** (Fragmin), and **sodium** pentosanpolysulfate have been investigated with regard to their anticoagulant effects in vitro and ex vivo and in an animal thrombosis model in which rat mesenteric venules are damaged by defined laser energy. GAG 262 and pentosanpolysulfate had a markedly reduced anticoagulant effect compared to heparin, Fragmin, and the supersulfated low-**mol.-wt.** heparin fragment. Similarly, the doses necessary to inhibit thrombus formation in the laser model were much higher for GAG 262 and for pentosanpolysulfate compared to heparin and the low-**mol.-wt.** heparin Fragmin, but much lower for the supersulfated heparin fragment. The antithrombotic effect of the low-**mol.-wt.** heparin Fragmin and the supersulfated heparin fragment after s.c. injection lasted much longer than the ex vivo detectable anticoagulant effect. Although some correlation between the antithrombotic and the anticoagulant effect in the laser model is evident, there seems to be no direct correlation between amt. and duration of factor **IIa** or factor **Xa** inhibition and extent and duration of the inhibition of thrombus formation.

=> d ibib abs hitstr 13

L103 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:516061 HCAPLUS
DOCUMENT NUMBER: 109:116061
TITLE: Nasal pharmaceuticals containing low-**molecular**-**weight** heparin and a fusidate.
INVENTOR(S): Johansen, Kristian Betton
PATENT ASSIGNEE(S): Leo Pharmaceutical Products Ltd., Den.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8707504	A1	19871217	WO 1987-DK65	19870601
W: DK, JP, US				
RW: BE, DE, FR, GB, IT, LU, NL, SE				
EP 270639	A1	19880615	EP 1987-904031	19870601
R: BE, DE, FR, GB, IT, LU, NL, SE				
JP 63503542	T2	19881222	JP 1987-503817	19870601
DK 8800385	A	19880127	DK 1988-385	19880127
PRIORITY APPLN. INFO.:			GB 1986-14189	19860611
			WO 1987-DK65	19870601

GI



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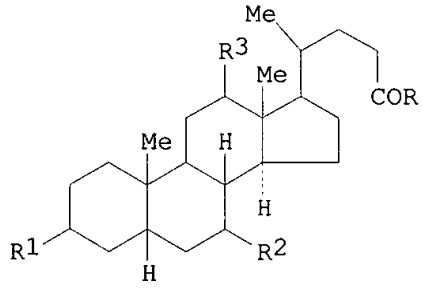

II

AB Pharmaceuticals contain a nordammarane deriv. (I; R = OH, NHZ; Z = alkyl or aryl optionally substituted by CO2, SO3, NH4+; X = H, OH, alkoxy, acyloxy, thioalkyl, thioacyl, halo; Y = OH, alkoxy, acyloxy, halo, alkoxysulfonyl, aryloxysulfonyl; the broken line indicates optional double bond) or a cholane analog (II; R as defined above; R1-R3 = H, OH whereby not all R1-R3 can be H simultaneously) as a nasal absorption enhancer and low-**mol**.-**wt**. heparin (III). Rabbits were administered a soln. contg. 7.5% (wt./vol.) III, 43 mM phosphate buffer, 130 mM NaCl,

15% (wt./vol.) EtOH, and 1% (wt./vol.) Na tauro-24,25-dihydrofusidate into the nasal cavity. The amt. of III administered (i.v.) was 5 mg/kg and its bioavailability was 8.8% of administered dose compared with 2.0% without the absorption enhancer. The antifactor **Xa** activity in a rabbit was 0.03, 0.65, 0.28, 0.43, and 0.24 units/mL after 0, 5, 15, 30, and 60 min, whereas in another, receiving III alone it was 0.03, 0.23, 0, 0.03 units/mL after 0, 5, 15, and 30 min, resp.

=> d ibib abs hitstr 1

L113 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:748867 HCAPLUS
DOCUMENT NUMBER: 130:106770
TITLE: Purification and characterization of a glucuronyltransferase involved in the biosynthesis of the HNK-1 epitope on glycoproteins from rat brain
AUTHOR(S): Terayama, Koji; Seiki, Takashi; Nakamura, Akemi; Matsumori, Kanae; Ohta, Satoru; Oka, Shogo; Sugita, Mutsumi; Kawasaki, Toshisuke
CORPORATE SOURCE: Department of Biological Chemistry and CREST (Core Research for Evolutional Science and Technology) Project, Japan Science and Technology Corporation, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Journal of Biological Chemistry (1998), 273(46), 30295-30300
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The glucuronyltransferase involved in the biosynthesis of the HNK-1 epitope on glycoproteins was purified to an apparent homogeneity from the Nonidet P-40 ext. of 2-wk postnatal rat forebrain by sequential chromatogs. on CM-Sepharose CL-6B, UDP-GlcA-Sepharose 4B, asialo-orosomucoid-Sepharose 4B, Matrex gel Blue A, Mono Q, HiTrap chelating, and HiTrap **heparin** columns. The purified enzyme migrated as a 45-**kDa** protein upon SDS-polyacrylamide gel electrophoresis under reducing conditions, but eluted as a 90-**kDa** protein upon Superose gel filtration in the presence of Nonidet P-40, suggesting that the enzyme forms homodimers under non-denatured conditions. The enzyme transferred **glucuronic** acid to various glycoprotein acceptors bearing **terminal** N-acetyllactosamine structure such as asialo-orosomucoid, asialo-fetuin, and asialo-neural cell adhesion mol., whereas little activity was detected to paragloboside, a precursor glycolipid of the HNK-1 epitope on glycolipids. These results suggested that the enzyme is specifically assocd. with the biosynthesis of the HNK-1 epitope on glycoproteins. Sphingomyelin was specifically required for expression of the enzyme activity. Stearoyl-sphingomyelin (18:0) was the most effective, followed by palmitoyl-sphingomyelin (16:0) and lignoceroyl-sphingomyelin (24:0). Interestingly, activity was demonstrated only for sphingomyelin with a satd. fatty acid, i.e. not for that with an unsatd. fatty acid, regardless of the length of the acyl group.

IT **9005-49-6, Heparin,** biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(purifn. and characterization of a glucuronyltransferase involved in the biosynthesis of the HNK-1 epitope on glycoproteins from rat brain)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L113 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:698927 HCAPLUS
DOCUMENT NUMBER: 127:345242
TITLE: Serum amyloid P component binds to influenza A virus hemagglutinin and inhibits the virus infection in vitro
AUTHOR(S): Andersen, O.; Ravn, K. Vilsgaard; Sorensen, I. Juul; Jonson, G.; Nielsen, E. Holm; Svehag, S. -E.
CORPORATE SOURCE: Department of Infectious Diseases, Odense University, Odense, DK-5000, Den.
SOURCE: Scandinavian Journal of Immunology (1997), 46(4), 331-337
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serum amyloid P component (SAP) is a member of the phylogenetically conserved and structurally related group of proteins called pentraxins. SAP exhibits multispecific calcium-dependent binding to oligosaccharides with **terminal** N-acetyl-galactosamine, mannose and **glucuronic** acid. The authors report that SAP can bind to influenza A virus and inhibit agglutination of erythrocytes mediated by the virus subtypes H1N1, H2N2 and H3N2. SAP also inhibits the prodn. of hemagglutinin (HA) and the cytopathogenic effect of influenza A virus in MDCK cells. The binding of SAP to the virus requires physiol. calcium concns. and is blocked by specific SAP antibodies. Denaturated and renaturated SAP retained inhibition of HA. Electron microscopy shows Ca2+-dependent binding of SAP to spikes on the viral envelope and immunoblotting indicates that SAP binds to a 50-55 **kDa** peptide corresponding to the mass of the HA1 peptide. Of several monosaccharides tested only D-mannose interfered with SAP's inhibition of both HA and infectivity. The glycosaminoglycans **heparan** sulfate and **heparin**, which bind SAP, reduced SAPs binding to the virus. The results indicate that the inhibition by SAP is due to steric effects when SAP binds to terminal mannose on oligosaccharides localized close to the sialic acid-binding site of the HA trimer.

IT **9005-49-6, Heparin,** biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(serum amyloid P component binding to influenza A virus hemagglutinin reactivity with)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 3

L113 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:574339 HCAPLUS
DOCUMENT NUMBER: 103:174339
TITLE: Distribution of glucuronic and iduronic acid units in **heparin** chains
AUTHOR(S): Radoff, Steven; Danishefsky, Isidore
CORPORATE SOURCE: Dep. Biochem., New York Med. Coll., Valhalla, NY, 10595, USA
SOURCE: J. Biol. Chem. (1985), 260(28), 15106-11
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The distribution of glucuronic and iduronic acid within the chains of anticoagulant-active and -inactive beef lung **heparin** was investigated. A fraction with an av. **mol. wt.** of 19,500 was isolated from the heterodisperse mixt. and then sepd. into active and inactive components by affinity chromatog. Each sample was linked through its reducing terminus to tyramine, reduced with NaB3H4, and bound covalently to Sepharose via an azo bridge. The bound, reduced **heparin** was treated with a limited amt. of HNO2 and the degraded fragments were removed. The sections of the chain contiguous with the original reducing terminus were then detached from the insol. matrix by reaction with Na dithionite. The recovered polysaccharide was fractionated according to size on Sephadex G-200 and the amt. of each uronic acid in the individual fractions was detd. Inactive **heparin** showed a const. percentage of glucuronic acid in all fragments, i.e., .apprx.8.9% of the total uronic acid. With active **heparin**, the percentage of **glucuronic** acid increased with the distance from the reducing **terminus** of the polysaccharide chain, ranging 9.5-20% of the uronic acids. Thus, the biosynthesis of active **heparin** apparently involves unique reactions or specific processing of the macromol.

IT **9005-49-6**, biological studies
RL: BIOL (Biological study)
(glucuronate and iduronate distribution in, of lung, anticoagulant activity in relation to)

RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 4

L113 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:451764 HCAPLUS
DOCUMENT NUMBER: 103:51764
TITLE: Oligosaccharides generated by an endoglucuronidase are intermediates in the intracellular degradation of **heparan** sulfate proteoglycans
AUTHOR(S): Kjellen, Lena; Pertoft, Haakan; Oldberg, Aake; Hoeoek, Magnus
CORPORATE SOURCE: Biomed. Cent., Univ. Uppsala, Uppsala, Swed.
SOURCE: J. Biol. Chem. (1985), 260(14), 8416-22
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An intracellular **heparan** sulfate oligosaccharide was identified in rat hepatocytes cultured in the presence of [35S]sulfate. Pulse-chase expts. suggested that [35S]sulfate is first incorporated into **heparan** sulfate proteoglycans which are subsequently converted to the low-**mol.**-**wt.** component. The oligosaccharide (**mol. wt.** 7000) contained little or no protein and was also present in rat liver homogenates. Subcellular fractionation and d.-gradient centrifugation in Percoll of liver homogenates demonstrated that the oligosaccharide was present in lysosomes or in particles of similar distribution and buoyant d. Structural anal. of oligosaccharides isolated from a rat liver lysosomal fraction indicated that **glucuronic** acid is present in the reducing **end** of the oligosaccharide and that this residue is preferentially linked to an N-acetylated glucosamine unit. Apparently, the **heparan** sulfate oligosaccharide is generated through the action of a **heparan** sulfate-degrading endoglucuronidase previously found in human platelets and rat liver (Oldberg, A.; et al., 1980).

=> d ibib abs hitstr 5

L113 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:540766 HCAPLUS
DOCUMENT NUMBER: 97:140766
TITLE: Purification and properties of human platelet heparitinase
AUTHOR(S): Oosta, Gary M.; Favreau, Leonard V.; Beeler, David L.; Rosenberg, Robert D.
CORPORATE SOURCE: Harvard Med. Sch., Beth Israel Hosp., Boston, MA, 02115, USA
SOURCE: J. Biol. Chem. (1982), 257(19), 11249-55
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heparitinase (I), an endoglycosidase which cleaves **heparin** and **heparan** sulfate, was isolated from outdated human blood platelets by freeze-thaw solubilization, **heparin**-Sepharose chromatog., DEAE-cellulose chromatog., hydroxylapatite chromatog., octyl-agarose chromatog., con A-Sepharose chromatog., and Sephacryl S-200 gel filtration. The overall extent of purifn. of platelet I was .apprx.240,000-fold and the overall yield was .apprx.5.6% as compared to the initial freeze-thaw solubilization prepn. The final product was phys. homogeneous as judged by disc gel electrophoresis at acidic pH as well as by gel filtration chromatog. and exhibited an apparent **mol. wt.** of .apprx.134,000. I was apparently present within platelet lysosomes. The biol. potency of I was examd. as a function of pH. I was max. active at pH 5.5-7.5. However, I possessed minimal ability to cleave **heparin** at pH <4.0 or >9.0. The substrate specificity of I was detd. by identifying susceptible linkages within the **heparin** mol. that could be cleaved by the above component. Apparently, I was only able to hydrolyze glucuronsyl-glucosamine linkages. Investigation of the structure of the disaccharide which lies on the nonreducing **end** of the cleaved **glucuronic** acid residue suggested that N-sulfation of the glucosamine moiety or ester sulfation of the adjacent iduronic acid groups were not essential for bond scission.
IT **9005-49-6**, biological studies
RL: RCT (Reactant)
(cleavage of, by heparitinase of human blood platelets, pH effect on)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 6

L113 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:110167 HCAPLUS
DOCUMENT NUMBER: 96:110167
TITLE: Improved anticoagulant substance
INVENTOR(S): Barnett, William E.
PATENT ASSIGNEE(S): Riker Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8103276	A1	19811126	WO 1981-US519	19810417
W: AU, DK, JP, NO				
RW: AT, CH, DE, FR, GB, LU, NL, SE				
US 4351938	A	19820928	US 1980-151163	19800519
AU 8171716	A1	19811207	AU 1981-71716	19810417
JP 57500612	T2	19820408	JP 1981-501646	19810417
EP 53612	A1	19820616	EP 1981-901249	19810417
R: AT, CH, DE, FR, GB, LU, NL, SE				
ZA 8103321	A	19820526	ZA 1981-3321	19810518
BE 888864	A1	19811119	BE 1981-204833	19810519
DK 8200189	A	19820118	DK 1982-189	19820118
NO 8200136	A	19820118	NO 1982-136	19820118
US 4438261	A	19840320	US 1982-384032	19820601
PRIORITY APPLN. INFO.:			US 1980-151163	19800519
			WO 1981-US519	19810417

AB A partially depolymd. **heparin** product, which has an av. **mol. wt.** of 2000-7000 daltons, is obtained by treating a com. **heparin** salt with HNO2 under controlled conditions. This product can be used for inhibiting blood coagulation. Thus, 20 g com. Na **heparin** [9041-08-1] was dissolved in 1 L aq. AcOH (1% by vol.) and treated with 160 mL 0.4% NaNO2 soln. and the mixt. stirred at 20.degree. for 3.5 h. The soln. was then frozen, and lyophilized to yield 19.8 g granular white solid. The **mol. wt.**, as detd. by high-performance liq. chromatog. with 1.5M NaCl as the mobile phase, is 2400-6100 Daltons, the polydispersity is 1.9 and wt.% of the sample having **mol. wt.** >15,000 D is 4.2. The USP potency is 41.0 units/mg. The **end** group anal. showed the presence of anhydromannose, iduronic acid and **glucuronic** acid at concns. 98, 39.6, and 19.5 nMol/mg, resp.

=> d ibib abs hitstr 7

L113 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:492922 HCAPLUS
DOCUMENT NUMBER: 95:92922
TITLE: Biosynthesis of **heparin**. Transfer of N-acetylglucosamine to **heparan** sulfate oligosaccharides
AUTHOR(S): Forsee, W. Thomas; Roden, Lennart
CORPORATE SOURCE: Inst. Dent. Res., Univ. Alabama, Birmingham, AL, 35294, USA
SOURCE: J. Biol. Chem. (1981), 256(14), 7240-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The N-acetylglucosaminyltransferase which acts in conjunction with a glucuronosyltransferase in the biosynthesis of the polysaccharide backbone of **heparin** was investigated. Substrates for the enzyme were prepd. from a low-sulfated, glucuronic acid-rich **heparan** sulfate fraction, which was desulfated and subsequently treated with HNO2; the products of the deaminative cleavage were fractionated by gel chromatog. on Sephadex G-25, yielding a series of oligosaccharides which ranged from di- to dodecasaccharides. Characterization of the tetra-, hexa-, and octasaccharide fractions by digestion with .beta.-glucuronidase showed that close to 60% of the nonreducing **termini** in each fraction was occupied by **glucuronic** acid. When incubated with a solubilized enzyme prepn. from a mouse mastocytoma which has been partially purified by chromatog. on DEAE-cellulose, all oligosaccharide fractions except the disaccharides served as acceptors for N-acetylglucosaminyl transfer. Anal. of the products showed that transfer of a single N-acetylglucosamine residue had occurred and that the newly formed glycosidic linkage was of the .alpha. configuration. Acceptor activity was abolished by digestion with .beta.-glucuronidase, indicating that glucuronic acid units, but not iduronic acid residues, could serve as substrates. The enzyme exhibited decreasing Km values of 8.7, 1.3, and 0.07 mM for the tetra-, hexa-, and octasaccharides, resp., suggesting that the affinity of the transferase for the growing polysaccharide may increase markedly in the early stages of polymn. When the octasaccharide fraction was incubated with a particulate microsomal enzyme prepn. in the presence of both UDP-N-acetylglucosamine and UDP-glucuronic acid, it served as a primer for the formation of a high-**mol.-wt** . product.

IT **9005-49-6**, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, substrates for acetylglucoaminyltransferase in)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 8

L113 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:53939 HCAPLUS
DOCUMENT NUMBER: 92:53939
TITLE: Substrate specificity of a **heparan** sulfate-degrading endoglucuronidase from human placenta
AUTHOR(S): Klein, Udo; Von Figura, Kurt
CORPORATE SOURCE: Physiol.-Chem. Inst., Univ. Muenster, Muenster, D-4400, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Z. Physiol. Chem. (1979), 360(10), 1465-71
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A **heparan** sulfate-degrading endoglucuronidase was isolated from human placenta and partially purified by affinity chromatog. of **heparin** sulfate-Sepharose 4B. The endoglucuronidase had a **mol. wt.** of .apprx.100,000 estd. by gel chromatog. and a broad pH optimum between pH 4 and pH 6. Carboxyl-reduced **heparan** sulfate was not split by partially purified endoglucuronidase, but inhibited the action of that enzyme towards nonmodified **heparan** sulfate. Low-**mol.-wt.-** **heparan** sulfate (**mol. wt.** .apprxeq.3000) was not attacked by the endoglucuronidase. N-Desulfated **heparan** sulfate and **heparin** were only weak substrates. The amino sugar adjacent to the **glucuronic** acid residue appearing at the reducing **terminal** of **heparan** sulfate fragments liberated by the endoglucuronidase appears to be exclusively N-acetylated glucosamine.

IT **9005-49-6**, biological studies
RL: PRP (Properties)
(degrdn. of, by endoglucuronidase of placenta)

RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 9

L113 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:179925 HCAPLUS
DOCUMENT NUMBER: 90:179925
TITLE: Correlation between structure and function of **heparin**
AUTHOR(S): Rosenberg, Robert D.; Lam, Lun
CORPORATE SOURCE: Sidney Farber Cancer Inst., Beth Israel Hosp., Boston, Mass., USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1979), 76(3), 1218-22
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crude porcine **heparin** [**9005-49-6**] was fractionated to obtain highly active as well as relatively inactive species of **mol**. **wt**. .apprxeq.7000 with specific anticoagulant activities of 360 and 12 units/mg, resp. Nitrous acid degrdn. of both of these polymers yielded a tetrasaccharide fraction, I.beta., that contained equimolar amts. of iduronic and **glucuronic** acids, possessed an internal N-acetylated glucosamine, and carried anhydromannitol at the reducing **end** position. The I.beta. tetrasaccharide derived from the highly active **heparin**, I.beta.a, was recovered in a yield of 1.1 mol/7000 daltons. At least 95% of the I.beta.a was a single structure that consisted of the following unique monosaccharide sequence: L-iduronic acid .fwdarw. N-acetyl-D-glucosamine-6-sulfate .fwdarw. D-glucuronic acid .fwdarw. D-glucosamine-N,6-disulfate. The I.beta. tetrasaccharide fraction from relatively inactive mucopolysaccharide, I.beta.i, was recovered in a yield of 0.3 mol/7000 daltons and was a mixt. of several components. Only 8.5% of the I.beta.i tetrasaccharide fraction exhibited the same uronic acid placement and sulfate group position found in I.beta.a. Thus, 2.6% of relatively inactive mucopolysaccharide mols. contain the unique tetrasaccharide sequence found within each mol. of highly active **heparin**. Given the correlation between abundance of this unique I.beta.a tetrasaccharide sequence and biol. potency, this structure represents the crit. site responsible for anticoagulant activity.

IT **9005-49-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticoagulant activity of, mol. structure in relation to)

RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 10

L113 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:540209 HCAPLUS
DOCUMENT NUMBER: 89:140209
TITLE: Structure-function relationships of **heparin** species
AUTHOR(S): Rosenberg, Robert D.; Armand, Gerard; Lam, Lun
CORPORATE SOURCE: Sidney Farber Cancer Inst., Beth Israel Hosp., Boston, Mass., USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1978), 75(7), 3065-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Porcine **heparin** species of low **mol. wt.**, with an av. specific anticoagulant activity of 96 units/mg were fractionated by affinity chromatog. Highly active and relatively inactive prepns. of similar size were obtained with specific anticoagulant activities of 360 and 4 units/mg, resp. The highly active **heparin** fraction possessed 1.1 addnl. residues of glucuronic acid [6556-12-3] and 1.5 fewer residues of N-sulfated glucosamine per mol. compared to the relatively inactive species. This decrease in N-sulfated glucosamine appeared to be secondary to a corresponding increase in N-acetylated glucosamine. This form also contained a tetrasaccharide sequence with a N-sulfated glucosamine at its reducing **end** as well as equiv. amts. of **glucuronic** acid and iduronic acid [3402-98-0]. The internal glucosamine residue of this sequence appeared to be N-acetylated. Sufficient amts. of this tetrasaccharide sequence were present within the highly active prepn. such that each mol. may be endowed with this structure. The relatively inactive product contained a decreased quantity of this tetrasaccharide sequence such that only .simeq.20% of these mols. may possess this structure. The mean distance between nonsulfated uronic acid residues of the highly active species was smaller than that sepg. similar residues of the relatively inactive product. In addn., a larger no. of the nonsulfated uronic acid residues of the highly active material appeared either to be present in a restricted region of the mol. sepd. only by glucosamine residues or to be located at pentultimate positions within the polysaccharide chain.

IT **9005-49-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(anticoagulant activity of fractions of)

RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 11

L113 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1975:166426 HCAPLUS
DOCUMENT NUMBER: 82:166426
TITLE: Cleavage of macromolecular **heparin** by an enzyme from mouse mastocytoma
AUTHOR(S): Ogren, Soren; Lindahl, Ulf
CORPORATE SOURCE: Inst. Med. Chem., Univ. Uppsala, Uppsala, Swed.
SOURCE: J. Biol. Chem. (1975), 250(7), 2690-7
CODEN: JBCHA3
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Heparinase**, isolated from a transplantable mouse mastocytoma, degraded macromol., 35S-labeled, mastocytomal **heparin** (Kav .apprx.0.25) to products similar in size to com. **heparin** (Kav .apprx.0.85), apparently by nonrandom cleavage of a limited no. of glycosidic linkages/mol. Prolonged incubation times did not result in further product degrdn. No significant depolymerizing activity was obsd. with any other glycosaminoglycan tested. The pH optimum for degrdn. of macromol. **heparin** was .apprx. pH 5. The nature of the linkage cleaved by the **heparinase** was investigated by redn. of nonlabeled polysaccharide degrdn. products with Na borohydride. The degraded chains (but not the macromol substrate) incorporated significant amts. of tritium. An essentially monodisperse fraction of the labeled, degraded **heparin** had a **mol. wt.** of 14,500.
By relating the **mol. wt.** to the specific activity of the prepn., the amt. of reducible groups was calcd. as .apprx.1/mol. The 3H-labeled **heparin** was degraded to monosaccharides by a combination of acid hydrolysis and cleavage due to deamination with nitrous acid. Anal. of the degrdn. products showed a major radioactive component which behaved like L-gulonic acid. Since tritiated gulonic acid would be the expected redn. product of a polysaccharide mol. contg. a **glucuronic** acid residue in **terminal** position, these results tentatively suggest that **heparinase** is an endoglucuronidase. By direct deaminative cleavage of the 3H-labeled **heparin**, the glucosamine unit in the penultimate position was 52% N-sulfated and 48% N-acetylated. As only 14% of the glucosamine was N-acetylated in the macromol. **heparin** substrate the cleavage of this polysaccharide by the **heparinase** apparently occurs in regions more abundant in N-acetylated glucosamine residues than other portions of the mol. The possibility that formation and degrdn. of macromol. **heparin** occurs in mammalian species other than rodents is discussed.

=> d ibib abs hitstr 12

L113 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:466666 HCAPLUS
DOCUMENT NUMBER: 65:66666
ORIGINAL REFERENCE NO.: 65:12451b-f
TITLE: The carbohydrate-protein linkage in the protein complex of acid mucopolysaccharides
AUTHOR(S): Roden, Lennart
CORPORATE SOURCE: Univ. of Chicago
SOURCE: Struct. Function Connective Skeletal Tissue, Proc., St. Andrews, Scot. (1965), Volume Date 1964 141-5
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two crude glycopeptide fractions were sepd. by gel filtration on Sephadex G-50. The fraction with **mol. wt.** .apprx.1800 contained approx. 40% of its hexosamine as glucosamine, indicating the presence of a relatively large portion of keratosulfate. The lesser fraction, **mol. wt.** .apprx.1100, contg. little glucosamine had a molar ratio of uronic acid to hexosamine of 2:1. This fraction contained galactose and xylose. The molar ratio of uronic acid to galactose to xylose was approx. 2:2:1. Xylose was probably involved in the carbohydrate-protein linkage. The glycopeptides contained a **terminal** trisaccharide unit, **glucuronic** acid-**galactosamineglucuronic** acid-, from the chondroitin 4-sulfate chains. A disaccharide, composed of glucuronic acid and galactose linked by a .beta.-glucuronidic linkage, was isolated, upon hydrolysis, from chondroitin 4-sulfate glycopeptides. The galactose moiety was at the reducing end of this substance; the linkage was either 1 .fwdarw. 3 or 1 .fwdarw. 4. Thus a glucuronosyl galactose residue was a structural unit in the carbohydrate-protein linkage region. The analyses of the products obtained by mild acid hydrolysis of chondroitin 4-sulfate glycopeptides and by periodate oxidn. of xylosylserine indicated that xylose was linked by a glycosidic linkage to the OH group of serine. In peptide-contg. **heparin** prepns. serine was the major amino acid and in certain prepns. it was the only amino acid present in significant amts. Galactose and xylose were also present in such **heparin** samples. Mild acid hydrolysis of **heparin** contg. serine as the major amino acid produced 2 carbohydrateserine compds., identical in compn. and properties with the serine-contg. compds. obtained from chondroitin 4-sulfate glycopeptides. **Heparin** in the native state was linked to protein in a manner similar to that of chondroitin 4-sulfate. A trisaccharide, galactosylgalactosylxylose, was isolated from **heparin**. The quant. analyses of the chondroitin 4-sulfate glycopeptides also indicated that 2 galactose mols. might be involved in the linkage area. The following general arrangement was suggested for the complexes studied: uronic acid-hexosamine-glucuronic acidgalactose-galactose-xylose-serine.

=> d ibib abs hitstr

L112 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:103246 HCAPLUS
DOCUMENT NUMBER: 116:103246
TITLE: Proton NMR spectroscopic studies on the interactions between human plasma antithrombin III and defined low **molecular weight heparin** fragments
AUTHOR(S): Horne, Angela; Gettins, Peter
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37232-0146, USA
SOURCE: Biochemistry (1992), 31(8), 2286-94
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of length and compn. upon the antithrombin-binding properties of **heparin** were investigated for 2 series of structurally related **heparin** oligosaccharides. Each series consisted of a tetrasaccharide, hexasaccharide, and octasaccharide **heparin** fragment composed of alternating hexuronic acid (either iduronate 2-sulfate or glucuronate) and glucosamine 6,N-disulfate residues. These 2 series represented dominant structural motifs in intact **heparin** and differed from each other by the presence of a **glucuronic** acid in one series in place of an iduronate 2-sulfate residue penultimate to the reducing **end** of the fragment. Perturbations to the 1H resonances in the NMR spectrum of antithrombin upon binding of the 2 series of **heparin** fragments were compared to those generated by intact **heparin** binding, as well as to the effects of binding of a synthetic high-affinity pentasaccharide. All of the **heparin** fragments examd. appeared to bind to antithrombin at the same site. Three of the **heparin** fragments produced almost identical perturbations in the antithrombin 1H NMR spectrum compared to binding of intact **heparin**, including perturbations of resonances from Trp-49. This indicated that neither the glucuronic acid nor the trisulfated glucosamine residue (structural elements known to be part of the high-affinity **heparin** motif) are necessary for the majority of the conformational changes induced upon **heparin** fragment binding to antithrombin. However, the low anticoagulant activity of these fragments indicated that the changes in protein conformation upon fragment binding, as manifested by these 1H resonance perturbations, are not sufficient for catalytic activation of the inhibitor. Since there were few differences between the difference spectra generated by active **heparin** (either pentasaccharide or the intact species) as compared to the inactive **heparin** fragments, further limited conformational changes that arise from the presence of elements of the high-affinity motif that are absent in the **heparin** fragments considered here must be necessary for inhibitor activation by **heparin.**

IT **9005-49-6, Heparin,** biological studies
RL: BIOL (Biological study)
(antithrombin III of human interaction with, protein conformation and activity in relation to)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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L112 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
CC 13-5 (Mammalian Biochemistry)
Section cross-reference(s): 1
ST antithrombin interaction **heparin** fragment NMR
IT Molecular structure-biological activity relationship
(antithrombin-activating, of **heparin** low-**mol.**-**wt.** fragments)
IT Conformation and Conformers
(of antithrombin III, of human, low-**mol.**-**wt.** **heparin** fragments effect on)
IT Kinetics, enzymic
(of inhibition, of blood-coagulation factor **Xa** by human antithrombin III, low-**mol.**-**wt.** **heparin** fragments effect on)
IT **9005-49-6**, **Heparin**, biological studies
RL: BIOL (Biological study)
(antithrombin III of human interaction with, protein conformation and activity in relation to)
IT 89847-99-4 89872-05-9 121596-31-4 138459-88-8 138459-89-9 138459-90-2
RL: BIOL (Biological study)
(antithrombin III of human interaction with, protein conformation and activity response to, oligosaccharide structure in relation to)
IT 9000-94-6, Antithrombin
RL: BIOL (Biological study)
(**heparin** low-**mol.**-**wt.** fragments interaction with, of human, protein conformation and activity in relation to)
IT 9002-05-5, Blood-coagulation factor **Xa**
RL: BIOL (Biological study)
(inhibition of, by antithrombin III of human, kinetics of, low-**mol.**-**wt.** **heparin** fragments effect on)

=> d ibib abs hitstr 1

L56 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:137173 HCAPLUS
DOCUMENT NUMBER: 134:178396
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013264	A	20020416	BR 2000-13264	20000727
PRIORITY APPLN. INFO.:			IT 1999-MI1817 A	19990812
			WO 2000-EP7225 W	20000727

OTHER SOURCE(S): MARPAT 134:178396

AB Compds. or their salts of general formula (I): A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 = (CO)t or (X)t', wherein X = O, S, NR1c, R1c is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB -X2-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT **9005-49-6**, Dalteparin, reactions
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(antithrombotic; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Connective Tissue Research 1975, vol. 3. 73-79.

=> d ibib abs hitstr 2

L56 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:742057 HCAPLUS
DOCUMENT NUMBER: 133:309791
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061541	A2	20001019	WO 2000-EP3239	20000411
WO 2000061541	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311923	B1	20020320	IT 1999-MI752	19990413
BR 2000009703	A	20020108	BR 2000-9703	20000411
EP 1169298	A2	20020109	EP 2000-926870	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001004928	A	20011213	NO 2001-4928	20011010

PRIORITY APPLN. INFO.: IT 1999-MI752 A 19990413
WO 2000-EP3239 W 20000411
OTHER SOURCE(S): MARPAT 133:309791
AB Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.
IT **9005-49-6**, Dalteparin, reactions
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(antithrombotic; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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L56 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
IT 50-59-9, Cephaloridine 54-85-3, Isoniazid 56-75-7, Chloramphenicol 57-62-5 57-67-0, **Sulfaguanidine** 57-68-1, Sulfamethazine 57-92-1, Streptomycin, reactions 60-54-8, Tetracycline 61-24-5, Cephalosporin C 61-33-6, Benzyl penicillinic acid, reactions 61-72-3,

Cloxacillin 63-74-1, Sulfanilamide 65-49-6, p-Aminosalicylic acid 66-79-5, Oxacillin 68-35-9, Sulfadiazine 68-41-7, Cycloserine 72-14-0, Sulfathiazole 74-55-5, Ethambutol 74-79-3, Arginine, reactions 79-57-2, Oxytetracycline 80-02-4, 2-p-Sulfanilylanilinoethanol 80-03-5, Acediasulfone 80-08-0, Dapsone 80-32-0, Sulfachlorpyridazine 80-35-3, Sulfamethoxypyridazine 87-08-1, Penicillin V 87-09-2, Penicillin O 94-19-9, Sulfaethidole 103-12-8, Sulfamidochrysoidine 113-98-4, Penicillin G potassium 114-07-8, Erythromycin 115-68-4, Sulfadicramide 116-42-7, Sulfaproxyline 116-44-9, Sulfapyrazine 119-59-5, 4,4'-Sulfinyldianiline 120-34-3, N-Sulfanilyl-3,4-xylamide 122-11-2, Sulfadimethoxine 127-33-3, Demeclocycline 127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-79-7, Sulfamerazine 128-46-1, Dihydrostreptomycin 130-16-5, Cloxyquin 132-92-3, Methicillin sodium 132-93-4, Phenethicillin potassium 133-11-9, Phenyl aminosalicylate 138-39-6, Mafenide 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 144-83-2, Sulfapyridine 152-47-6, Sulfalene 153-61-7, Cephalothin 154-21-2, Lincomycin 303-81-1, Novobiocin 389-08-2 443-48-1, Metronidazole 473-30-3, Thiazolsulfone 485-41-6, Sulfachrysoidine 495-84-1, Salinazid 515-49-1, Sulfathiourea 515-59-3, Sulfamethylthiazole 515-64-0, Sulfisomidine 525-94-0, Penicillin N 526-08-9, Sulfaphenazole 547-44-4, Sulfanilylurea 547-52-4, N4-Sulfanilylsulfanilamide 547-53-5, 4'-(Methylsulfamoyl)sulfanilanilide 551-27-9, Propicillin 599-88-2, Sulfaperine 651-06-9, Sulfameter 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 751-97-3, Rolitetracycline 808-26-4, Sancycline 914-00-1, Methacycline 992-21-2, Lymecycline 1110-80-1, Pipacycline 1181-54-0, Clomocycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 1596-63-0, Quinacillin 1614-20-6, Nifurprazine 1695-77-8, Spectinomycin 1926-49-4, Clometocillin 1984-94-7, Sulfasymazine 2013-58-3, Meclocycline 2030-63-9, Clofazimine 2315-08-4, Salazosulfadimidine 2447-57-6, Sulfadoxine 2750-76-7, Rifamide 2751-09-9, Troleandomycin 2779-55-7, Opiniazide 3116-76-5, Dicloxacillin 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3577-01-3, Cephaloglycin 3590-05-4, Acetyl sulfamethoxypyrazine 3691-74-5, Glyconiazide 3772-76-7, Sulfamethomidine 3922-90-5, Oleandomycin 4008-48-4, Nitroxoline 4393-19-5, p-Sulfanilylbenzyl amine 4564-87-8, Carbomycin 4697-36-3, Carbenicillin 5250-39-5, Floxacillin 5934-14-5, Succisulfone 6202-21-7, 4-Sulfanilamidosalicylic acid 6489-97-0, Metampicillin 6946-29-8, p-Aminosalicylic acid hydrazide 6998-60-3, Rifamycin 7542-37-2, Paromomycin 8025-81-8, Spiramycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 11006-76-1, Virginiamycin 12650-69-0, Mupirocin 13411-16-0, Nifurpirinol 13838-08-9, Azidamfenicol 13898-58-3, Benzoylpas 13925-12-7, Myxin 15599-51-6, Apicycline 15686-71-2, Cephalexin 16545-11-2, Guamecycline 16846-24-5, Josamycin 17243-38-8, Azidocillin 17784-12-2, Sulfacytine 18323-44-9, Clindamycin 19562-30-2, Piromidic acid 23239-41-0, Cephacetrile sodium 23477-98-7, Sedecamycin 24356-60-3, Cephapirin sodium 25546-65-0, Ribostamycin 25953-19-9, Cefazolin 26086-49-7, Deoxydihydrostreptomycin 26774-90-3, Epicillin 26787-78-0, Amoxicillin 26973-24-0, Ceftezole 27031-08-9, Sulfaguanole 28657-80-9, Cinoxacin 32385-11-8, Sisomicin 32887-01-7, Amdinocillin 32909-92-5, Sulfametrole 32986-56-4, Tobramycin 32988-50-4, Viomycin 33103-22-9, Enviomycin 33404-78-3, Negamycin 33817-20-8, Pivampicillin 34444-01-4, Cefamandole 34493-98-6, Dibekacin 34787-01-4, Ticarcillin 35457-80-8, Midecamycin 35531-88-5, Carindacillin 35607-66-0, Cefoxitin 35834-26-5, Rosaramicin 37091-66-0, Azlocillin 37321-09-8, Apramycin 37517-28-5, Amikacin 38129-37-2, Bicozamycin 38821-53-3, Cephradine 41744-40-5, Sulbenicillin 42835-25-6, Flumequine 47747-56-8, Talampicillin 50370-12-2, Cefadroxil 50972-17-3,

Bacampicillin 51025-85-5, Arbekacin 51481-65-3, Mezlocillin 51627-14-6, Cefatrizine 51762-05-1, Cefroxadine 51940-44-4, Pipemidic acid 52093-21-7, Micronomicin 52152-93-9 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 55881-07-7, Miokamycin 56187-47-4, Cefazedone 56391-56-1, Netilmicin 56796-20-4, Cefmetazole 58001-44-8, Clavulanic acid 60925-61-3, Ceforanide 61270-58-4, Cefonicid 61379-65-5, Rifapentine 61477-96-1, Piperacillin 61622-34-2, Cefotiam 62013-04-1, Dirythromycin 62893-19-0, Cefoperazone 63358-49-6, Aspoxicillin 63469-19-2, Apalcillin 63527-52-6, Cefotaxime 63836-75-9, Cephalexin pivaloxymethyl ester 64221-86-9, Imipenem 64952-97-2, Moxalactam 65052-63-3, Cefetamet 65085-01-0, Cefmenoxime 66148-78-5, Temocillin 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 69739-16-8, Cefodizime 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 71426-83-0, Fortimicin 72558-82-8, Ceftazidime 72559-06-9, Rifabutine 73384-59-5 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 76470-66-1, Loracarbef 76497-13-7, Sultamicillin 76610-84-9, Cefbuperazone 78110-38-0, Aztreonam 79350-37-1, Cefixime 79548-73-5, Pirlimycin 79660-72-3, Fleroxacin 80370-57-6, Ceftiofur 80621-81-4, Rifaximin 81103-11-9, Clarithromycin 82219-78-1, Cefuzonam 82419-36-1, Ofloxacin 82547-58-8, Cefteram 83905-01-5, Azithromycin 84305-41-9, Cefminox 84845-57-8, Ritipenem 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 85721-33-1, Ciprofloxacin 86273-18-9, Lenampicillin 87239-81-4, Cefpodoxime proxetil 87638-04-8, Carumonam 87726-17-8, Panipenem 88040-23-7, Cefepime 88669-04-9, Trospectomycin 91832-40-5, Cefdinir 92665-29-7, Cefprozil 93106-60-6, Enrofloxacin 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7 98106-17-3, Difloxacin
RL: RCT (Reactant); RACT (Reactant or reagent)
(antibiotic; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

IT 58-32-2, Dipyridamole 68-90-6, Benziodarone 100-55-0, Nicotinyl alcohol 322-79-2, Triflusal 390-64-7, Prenylamine 395-28-8, Isoxsuprine 437-74-1, Xanthinol niacinate 447-41-6, Nylidrin 456-59-7, Cyclandelate 574-77-6, Papaveroline 987-78-0, Citicoline 3611-72-1, Clobenfurol 3703-79-5, Bamethan 5638-76-6, Betahistine 6621-47-2, Perhexiline **9005-49-6**, Dalteparin, reactions 13042-18-7, Fendiline 14838-15-4, Phenylpropanolamine 22103-14-6, Bufeniode 23210-56-2, Ifenprodil 36702-83-7, Tinofedrine 37270-89-6, Nadroparin calcium 42794-76-3, Midodrine 54767-75-8, Suloctidil 57475-17-9, Brovincamine 57653-27-7, Droprenilamine 63610-08-2, Indobufen 74863-84-6, Argatroban 78919-13-8, Iloprost 81110-73-8, Acetorphan 82571-53-7, Ozagrel 89667-40-3 110140-89-1, Ridogrel 144412-49-7, Lamifiban
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(antithrombotic; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

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L56 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:742053 HCAPLUS
DOCUMENT NUMBER: 133:310142
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311924	B1	20020320	IT 1999-MI753	19990413
BR 2000009702	A	20020108	BR 2000-9702	20000411
EP 1169294	A2	20020109	EP 2000-925203	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001004927	A	20011213	NO 2001-4927	20011010

PRIORITY APPLN. INFO.: IT 1999-MI753 A 19990413
WO 2000-EP3234 W 20000411
OTHER SOURCE(S): MARPAT 133:310142
AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepd. for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-.alpha.-methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepd. (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.
IT **9005-49-6**, Dalteparin, reactions
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(drug precursor)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d kwic 3

L56 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
IT 50-33-9, Phenylbutazone, reactions 50-44-2, Mercaptopurine 50-59-9,

Cephaloridine 50-91-9, Floxuridine 51-21-8, Fluorouracil 51-43-4, Epinephrine 51-45-6, Histamine, reactions 53-79-2, Puromycin 54-25-1, Azauridine 54-42-2, Idoxuridine 54-80-8, Pronethalol 54-85-3, Isoniazid 56-75-7, Chloramphenicol 56-81-5D, Glycerol, iodo deriv. 57-08-9, .epsilon.-Acetamidocaproic acid 57-22-7, Vincristine 57-27-2, Morphine, reactions 57-50-1, reactions 57-62-5 57-67-0, **Sulfaguanidine** 57-68-1, Sulfamethazine 57-92-1, Streptomycin, reactions 58-32-2, Dipyridamole 59-05-2, Methotrexate 60-00-4, Edetic acid, reactions 60-54-8, Tetracycline 61-24-5, CephalosporinC 61-33-6, Benzylpenicillinicacid, reactions 61-68-7, Mefenamicacid 61-72-3, Cloxacillin 63-74-1, Sulfanilamide 65-45-2 65-49-6, p-Aminosalicylic acid 66-79-5, Oxacillin 68-26-8, Vitamin A 68-35-9, Sulfadiazine 68-41-7, Cycloserine 68-88-2, Hydroxyzine 68-90-6, Benziodarone 69-33-0, Tubercidin 70-00-8, Trifluridine 72-14-0, Sulfathiazole 74-31-7, N,N'-Diphenyl-p-phenylenediamine 74-55-5, Ethambutol 74-79-3, Arginine, reactions 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 77-07-6, Levorphanol 79-57-2, Oxytetracycline 80-02-4, 2-p-Sulfanilylanilinoethanol 80-03-5, Acediasulfone 80-08-0, 4,4'-Sulfonyldianiline 80-32-0, Sulfachlorpyridazine 80-35-3, Sulfamethoxypyridazine 80-53-5, Terpin 84-16-2, Hexestrol 87-08-1, Penicillin V 87-09-2, Penicillin O 87-28-5, Glycolsalicylate 89-45-2, Salicylsulfuricacid 90-05-1, Guaiacol 91-53-2, Ethoxyquin 93-14-1, Guaifenesin 94-10-0, Ethoxazene 94-19-9, Sulfaethidole 97-53-0, Eugenol 97-54-1, Isoeugenol 98-54-4 98-92-0, Nicotinamide 100-55-0, Nicotinyl alcohol 101-91-7, 4'-Hydroxybutyranilide 103-12-8, Sulfamidochrysoidine 103-97-9, Phenocoll 110-17-8, Fumaric acid, reactions 111-17-1, 3,3'-Thiodipropionic acid 113-98-4, Penicillin G potassiumsalt 114-07-8, Erythromycin 115-02-6, Azaserine 115-68-4, Sulfadicramide 116-42-7, Sulfaproxyline 116-44-9, Sulfapyrazine 118-55-8, Phenyl salicylate 118-57-0, Acetaminosalol 119-98-2, Tocol 120-34-3, n-Sulfanilyl-3,4-xylamide 121-00-6, 3-tert-Butyl-4-hydroxyanisole 121-79-9, Propyl gallate 122-11-2, Sulfadimethoxine 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 127-07-1, Hydroxyurea 127-33-3, Demeclocycline 127-35-5, Phenazocine 127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-79-7, Sulfamerazine 128-37-0, 3,5-Di-tert-Butyl-4-hydroxytoluene, reactions 128-46-1, Dihydrostreptomycin 129-20-4, Oxyphenbutazone 130-16-5, Cloxyquin 132-60-5, Cinchophen 132-92-3, Methicillinsodium salt 132-93-4, Phenethicillin potassium salt 133-11-9, Phenylaminosalicylate 134-55-4, Phenylacetylsalicylate 136-70-9, Protokylol 138-52-3, Salicin 143-52-2, Metopon 144-14-9, Anileridine 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 144-83-2, Sulfapyridine 147-94-4, Cytarabine 148-24-3, 8-Quinolinol, reactions 148-82-3, Melphalan 152-47-6, Sulfalene 153-61-7, Cephalothin 154-21-2, Lincomycin 154-42-7, Thioguanine 157-03-9, 6-Diazo-5-oxo-L-norleucine 299-42-3, Ephedrine 302-79-4, Retinoic acid 303-81-1, Novobiocin 305-03-3, Chlorambucil 315-30-0, Allopurinol 320-67-2, Azacitidine 322-79-2, Triflusal 339-43-5, Carbutamide 359-83-1, Pentazocine 389-08-2 390-64-7, Prenylamine 395-28-8, Isoxsuprine 404-86-4, Capsaicine 427-00-9, Desomorphine 437-74-1, Xanthinol niacinate 443-48-1, Metronidazole 447-41-6, Nylidrin 456-59-7, Cyclandelate 458-35-5 458-37-7, Curcumin 466-97-7, Normorphine 466-99-9, Hydromorphone 468-56-4, Hydroxypethidine 473-30-3, Thiazolsulfone 477-30-5, Demecolcine 485-41-6, Sulfachrysoidine 486-79-3, Dipyrocetyl 487-48-9, Salacetamide 488-41-5, Mitobronitol 495-76-1, Piperonyl alcohol 495-84-1, Salinazid 497-75-6 498-71-5, Sobrerol 501-94-0, 4-Hydroxyphenethyl alcohol 509-60-4, Dihydromorphine 515-49-1, Sulfathiourea 515-59-3, Sulfamethylthiazole 515-64-0, Sulfisomidine 515-69-5, Bisabolol 518-28-5, Podophyllotoxin 519-37-9, Etofylline

525-94-0, Penicillin N 526-08-9, Sulfaphenazole 526-84-1, Dihydroxymaleic acid 530-08-5, Isoetharine 530-75-6, Acetylsalicylsalicylicacid 530-78-9, Flufenamicacid 533-73-3, Hydroxyhydroquinone 536-24-3, Ethylnorepinephrine 539-08-2, p-Lactophenetide 545-90-4, Dimepheptanol 547-44-4, Sulfanilylurea 547-52-4, Sulfanilylsulfanilamide 547-53-5 551-27-9, Propicillin 552-94-3, Salsalate 553-69-5, Benzenemethanol, ..alpha..-[(2-pyridinylamino)methyl]- 562-26-5, Phenoperidine 574-77-6, Papaveroline 576-68-1, Mannomustine 577-85-5, 3-Hydroxyflavone 581-64-6, Thionine 586-06-1, Metaproterenol 599-88-2, Sulfaperine 603-00-9, Proxyphylline 610-88-8 632-00-8, Sulfasomizole 635-65-4, Bilirubin, reactions 639-48-5, Nicomorphine 644-62-2, Meclofenamicacid 651-06-9, Sulfameter 652-37-9, Acefylline 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 751-97-3, Rolitetracycline 768-94-5, Amantadine 801-52-5, Porfiromycin 808-26-4, Sancycline 824-46-4, Methoxyhydroquinone 840-50-6, MADU 865-21-4, Vinblastine 959-10-4, Xenbucin 987-78-0, Citicoline 992-21-2, Lymecycline 1077-28-7, Thioctic acid 1083-57-4, Bucetin 1110-80-1, Pipacycline 1159-93-9, Clobenzepam 1174-11-4, Xenazoic acid 1181-54-0, Clomocycline 1400-61-9, Nystatin 1403-28-7, Carzinophilin 1403-66-3, Gentamicin 1404-04-2, Neomycin 1404-15-5, Nogalamycin 1406-18-4, Vitamin E 1503-53-3, 5-Bromosalicylic acid acetate 1531-12-0, Norlevorphanol 1553-60-2, Ibufenac 1596-63-0, Quinacillin 1614-20-6, Nifurprazine 1695-77-8, Spectinomycin 1853-37-8, Podophyllicacid 1926-49-4, Clometocillin 1953-02-2, Tiopronin 1984-94-7, Sulfasymazine 2013-58-3, Meclocycline 2016-63-9, Bamifylline 2030-63-9, Clofazimine 2055-44-9, Perisoxal 2179-16-0, Ninopterin 2315-08-4, Salazosulfadimidine 2316-64-5, Bromosaligenin 2363-58-8, Epitiostanol 2373-80-0, 3,4-Methylenedioxycinnamic acid 2447-57-6, Sulfadoxine 2750-76-7, Rifamide
RL: RCT (Reactant); RACT (Reactant or reagent)
(drug precursor)

IT 2751-09-9, Troleandomycin 2779-55-7, Opiniazide 2809-21-4, Etidronicacid 2933-94-0, Toliprolol 3056-17-5, Stavudine 3094-09-5, Doxifluridine 3116-76-5, Dicloxacillin 3215-70-1, Hexoprenaline 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3567-76-8 3572-43-8, Bromhexine 3577-01-3, Cephaloglycin 3590-05-4, Acetylsulfamethoxypyrazine 3611-72-1, Clobenfurol 3690-05-9, p-Coumaric alcohol 3691-74-5, Glyconiazide 3703-79-5, Bamethan 3733-81-1, Defosfamide 3734-52-9, Metazocine 3772-76-7, Sulfamethomidine 3811-25-4 3820-67-5, Glafenine 3922-90-5, Oleandomycin 3930-19-6, Streptonigrin 3930-20-9, Sotalol 4008-48-4, Nitroxoline 4097-22-7, Dideoxyadenosine 4393-19-5 4394-00-7, Niflumicacid 4564-87-8, Carbomycin 4697-36-3, Carbenicillin 4803-27-4, Anthramycin 5205-82-3, Bevoniummethylsulfate 5250-39-5, Floxacillin 5486-77-1, Alloclamide 5536-17-4, Vidarabine 5581-52-2, Thiamiprine 5633-20-5, Oxybutynin 5638-76-6, Betahistine 5728-52-9, Felbinac 5741-22-0, Moprolol 5934-14-5, Succisulfone 6064-83-1, Fosfosal 6135-36-0, 1-Butyl-3-methylurea 6202-21-7, 4-Sulfanilamidosalicylic acid 6452-71-7, Oxprenolol 6489-97-0, Metampicillin 6621-47-2, Perhexiline 6673-35-4, Practolol 6946-29-8, P-Aminosalicylicacidhydrazide 6998-60-3, Rifamycin 7413-36-7, Nifenalol 7481-89-2, Zalcitabine 7542-37-2, Paromomycin 8025-81-8, Spiramycin **9005-49-6**, Dalteparin, reactions 9041-08-1, Reviparin sodium 10118-90-8, Minocycline 10318-26-0, Mitolactol 11003-38-6, Capreomycin 11006-76-1, Virginiamycin 11120-15-3, Dermostatin 12650-69-0, Mupirocin 13042-18-7, Fendiline 13292-46-1, Rifampin 13392-18-2, Fenoterol 13392-28-4, Rimantadine 13411-16-0, Nifurpirinol 13523-86-9 13642-52-9, Soterenol 13655-52-2, Alprenolol 13665-88-8, Mopidamol 13710-19-5, Tolfenamicacid 13739-02-1, Diacerein 13741-18-9, Xibornol 13799-03-6, Protizinicacid 13838-08-9,

Azidamfenicol 13898-58-3, Benzoylpas 13925-12-7, Myxin 13946-02-6, Metron S 13993-65-2, Metiazinicacid 14556-46-8, Bupranolol 14838-15-4, Phenylpropanolamine 15176-29-1, Edoxudine 15307-79-6, Sodium diclofenac 15468-10-7, Oxidronic acid 15599-51-6, Apicycline 15686-71-2, Cephalexin 15722-48-2, Olsalazine 16110-51-3 16545-11-2, Guamecycline 16846-24-5, Josamycin 17243-38-8, Azidocillin 17737-65-4, Clonixin 17784-12-2, Sulfacytine 17969-20-9, Fenclozicacid 18046-21-4, Fentiazac 18323-44-9, Clindamycin 18378-89-7, Plicamycin 18471-20-0, Ditazol 18699-02-0, Actarit 18883-66-4, Streptozocin 19562-30-2, Piromidicacid 19767-45-4, Mesna 20168-99-4, Cinmetacin 20187-55-7, Bendazac 20594-83-6, Nalbuphine 20830-81-3, Daunorubicin 21256-18-8, Oxaprozin 21679-14-1, Fludarabine 22006-84-4, Denopterin 22071-15-4, Ketoprofen 22103-14-6, Bufeniode 22131-79-9, Alclofenac 22254-24-6, Ipratropiumbromide 22494-42-4, Diflunisal 22664-55-7, Metipranolol 22668-01-5, Etanidazole 23031-25-6, Terbutaline 23049-93-6, Enfenamic acid 23210-56-2, Ifenprodil 23239-41-0, Cephacetrilesodium 23477-98-7, Sedecamycin 23694-81-7, Mepindolol 23779-99-9, Floctafenine 24237-54-5, Tinoridine 24280-93-1, Mycophenolic acid 24356-60-3, Cephapirinsodium 25395-22-6, Salicylamide O acetic acid 25546-65-0, Ribostamycin 25803-14-9, Clometacin 25953-19-9, Cefazolin 26086-49-7, Deoxydihydrostreptomycin 26171-23-3, Tolmetin 26774-90-3, Epicillin 26787-78-0, Amoxicillin 26839-75-8, Timolol 26973-24-0, Ceftezole 27031-08-9, Sulfaguanole 27203-92-5, Tramadol 27470-51-5, Suxibuzone 27726-31-4, Pivcephalexin 27762-78-3, Kethoxal 28657-80-9, Cinoxacin 29122-68-7, Atenolol 29679-58-1, Fenoprofen 29767-20-2, Teniposide 30187-90-7, Xibenolol 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 30418-38-3, Tretoquinol 30516-87-1, Zidovudine 30544-47-9, Etofenamate 30653-83-9, Parsalmide 31127-82-9, Iodoxamide 31698-14-3, Ancitabine 31793-07-4, Pirprofen 31842-01-0, Indoprofen 32385-11-8, Sisomicin 32527-55-2, Tiaramide 32665-36-4, Eprozinol 32808-51-8, Bucloxic acid 32887-01-7, Amdinocillin 32909-92-5, Sulfametrole 32953-89-2, Rimiterol 32986-56-4, Tobramycin 32988-50-4, Viomycin 33005-95-7, Tiaprofenicacid 33069-62-4, Paclitaxel 33103-22-9, Enviomycin 33159-27-2, Ecabet 33369-31-2, Zomepirac 33404-78-3, Negamycin 33419-42-0, Etoposide 33817-20-8, Pivampicillin 33996-33-7, Oxaceprol 34148-01-1, Clidanac 34444-01-4, Cefamandole 34493-98-6, Dibekacin 34552-84-6, Isoxicam 34661-75-1, Urapidil 34675-84-8, Cetraxate 34787-01-4, Ticarcillin 34866-47-2, Carbuterol 34915-68-9, Bunitrolol 34919-98-7, Cetamolol 35457-80-8, Midecamycin 35531-88-5, Carindacillin 35607-66-0, Cefoxitin 36330-85-5, Fenbufen 36702-83-7, Tinofedrine 36791-04-5, Ribavirin 36894-69-6, Labetalol 36981-91-6, Fepradinol 37091-66-0, Azlocillin 37148-27-9, Clenbuterol 37321-09-8, Apramycin 37517-28-5, Amikacin 37517-30-9, Acebutolol 37762-06-4, Zaprinast 38129-37-2, Bicozamycin 38194-50-2, Sulindac 38363-40-5, Penbutolol 38677-81-5, Pirbuterol 38677-85-9, Flunixin 38821-53-3, Cephradine 39324-30-6, Pepstatin 39718-89-3, Alminoprofen 39809-25-1, Penciclovir 40391-99-9, Pamidronicacid 40828-46-4, Suprofen 41340-25-4, Etodolac 41570-61-0, Tulobuterol 41744-40-5, Sulbenicillin 42200-33-9, Nadolol 42408-82-2, Butorphanol 42779-82-8, Clopirac 42794-76-3, Midodrine 42835-25-6, Flumequine 47747-56-8, Talampicillin 50264-69-2, Lonidamine 50270-33-2, Isofezolac 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50935-04-1, Carubicin 50972-17-3, Bacampicillin 51025-85-5, Arbekacin 51384-51-1, Metoprolol 51395-42-7, Butedronic acid 51481-61-9, Cimetidine 51481-65-3, Mezlocillin 51579-82-9, Amfenac 51627-14-6, Cefatrizine 51762-05-1, Cefroxadine 51781-06-7, Carteolol 51940-44-4, Pipemidicacid 52081-33-1, Mitomycins 52093-21-7, Micronomicin

RL: **RCT (Reactant)**; RACT (Reactant or reagent)

(drug precursor)

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L56 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:477885 HCAPLUS
DOCUMENT NUMBER: 127:162048
TITLE: Modifications under basic conditions of the minor sequences of heparin containing 2,3- or 2,3,6-sulfated D-glucosamine residues
AUTHOR(S): Santini, Francesco; Bisio, Antonella; Guerrini, Marco; Yates, Edwin A.
CORPORATE SOURCE: Istituto di Chimica e Biochimica "G. Ronzoni", Milan, 20133, Italy
SOURCE: Carbohydrate Research (1997), 302(1-2), 103-108
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 1H NMR chem. shift assignments are reported for 2,3-di- or 2,3,6-tri-sulfated glucosamine in a sample of high affinity (for antithrombin III) heparin in three distinct environments. Following treatment in **strong basic** conditions the disappearance of these signals and the appearance of new signals consistent with the formation of N-sulfo-2,3-aziridine contg. amino sugar residues is demonstrated. Anti-factor Xa activity of sulfoaziridine heparin were performed using a chromogenic endpoint assay employing an accucolor heparin kit.
IT **9005-49-6**, Heparin, reactions
RL: **RCT (Reactant)**; RACT (Reactant or reagent)
(intramol. cyclocondensation aziridination of the minor sequences of heparin contg. 2,3- or 2,3,6-sulfated D-glucosamine residues)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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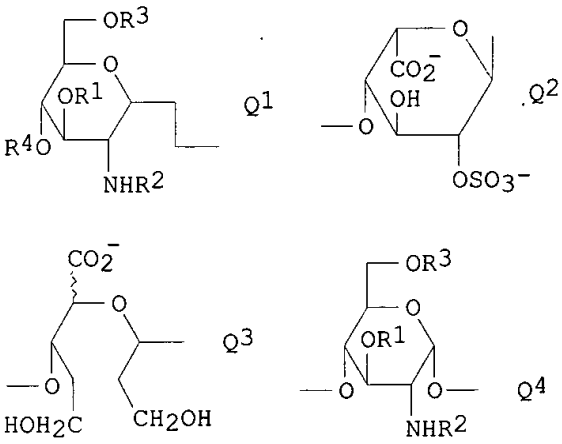
L56 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:417717 HCAPLUS
DOCUMENT NUMBER: 111:17717
TITLE: Low-molecular-weight heparins with a regular structure, their preparation and biological uses
INVENTOR(S): Lormeau, Jean Claude; Petitou, Maurice; Choay, Jean; SANOFI
PATENT ASSIGNEE(S): SANOFI, Fr.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 287477	A2	19881019	EP 1988-400928	19880415
EP 287477	A3	19890726		
EP 287477	B1	19941102		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2614026	A1	19881021	FR 1987-5457	19870416
FR 2614026	B1	19920417		
FI 8801783	A	19881017	FI 1988-1783	19880415
FI 88046	B	19921215		
FI 88046	C	19930325		
NO 8801660	A	19881017	NO 1988-1660	19880415
NO 170940	B	19920921		
NO 170940	C	19921230		
AU 8814663	A1	19881020	AU 1988-14663	19880415
AU 601566	B2	19900913		
JP 63278901	A2	19881116	JP 1988-91891	19880415
ZA 8802662	A	19881130	ZA 1988-2662	19880415
US 4990502	A	19910205	US 1988-181969	19880415 X
CA 1327968	A1	19940322	CA 1988-564296	19880415
DK 8802103	A	19881017	DK 1988-2103	19880418
DK 173982	B1	20020325		

PRIORITY APPLN. INFO.: FR 1987-5457 A 19870416
GI



AB A low-mol.-wt. heparin, R(XY)nR' [I; R = H, Q1; X = Q2, Q3; Y = Q4; R1 = H, SO3-; R2 = Ac, SO3- (.apprx.90%); R3 = H, SO3- (.apprx.70%); R4 = H, uronic acid; R' = H, natural uronic acid, oxidized uronic acid with aldehyde groups reduced to alcs.; n = 7-15], of .apprx.4800-9000 mol. wt., is prepd. by (1) treating an aq. soln. of heparin (0.5-5%, wt./vol.) with HIO4 (0.5-4%, wt./vol.) at pH 4.5-6.5 and 0-10.degree.; (2) treating the heparin chains obtained with 0.1-0.3N **strong base**; (3) treating the **depolymd**. fragments with a reducing agent; (4) eliminating the excess reducing agent and pptg. the fragments with a mineral salt and an alc.; (5) recovering the product and converting it to a pharmaceutically acceptable salt. I does not have anticoagulant activity and is useful as a medicament for regulating certain physiol. systems. Porcine heparin Na salt (10 g) was treated with NaIO4 at pH 5.0 and 4.degree. for 24 h in the dark, the residual IO4- was removed by dialysis, and the modified heparin was **depolymd**. with 10N soda for 3 h at 18-21.degree.. The product was reduced with NaBH4 and then fractionated by repeated pptn. with NaCl-contg. EtOH, to give 5.0 g product (IC 1772). IC 1772 inhibited the proliferation of rat smooth muscle cells in vitro and in vivo similarly to heparin std., inhibited the formation of complement C 3b-protein B complex with a 50% inhibitory concn. of 0.4 .mu.g/mL (heparin value = 0.5 .mu.g/mL), and administered i.v. to rabbits at 1 mg/kg had antithrombotic activity in all 10 animals.

IT **9005-49-6P**, Heparin, biological studies
RL: SPN (Synthetic preparation); PREP (Preparation)
(low-mol.-wt., modified, prepn. of)

RN 9005-49-6 HCAPLUS

CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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L56 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

IC ICM C08B037-10
ICS A61K031-725

CC 1-8 (Pharmacology)
Section cross-reference(s): 9, 15

ST heparin deriv antithrombotic complement inhibitor; smooth muscle inhibitor heparin deriv

IT Cell division
(by smooth muscle, low-mol.-wt. modified heparin inhibition of)
IT Anticoagulants and Antithrombotics
(low-mol.-wt. modified heparin)
IT Muscle
(smooth, proliferation of, low-mol.-wt. modified heparin inhibition of)
IT 80295-43-8D, Complement C 3b, factor B complexes 80295-62-1D, Complement factor B, complement C 3b complexes
RL: FORM (Formation, nonpreparative)
(formation of, low-mol.-wt. modified heparin inhibition of)
IT 9005-48-5P, Potassium heparin **9005-49-6P**, Heparin, biological studies 9041-08-1P, Sodium heparin 37270-89-6P, Calcium heparin 54479-70-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(low-mol.-wt., modified, prepn. of)

=> d ibib abs hitstr 6

L56 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:595609 HCAPLUS
DOCUMENT NUMBER: 107:195609
TITLE: Neutralization and binding of heparin by S protein/vitronectin in the inhibition of factor Xa by antithrombin III. Involvement of an inducible heparin-binding domain of S protein/vitronectin
AUTHOR(S): Preissner, Klaus T.; Mueller-Berghaus, Gert
CORPORATE SOURCE: Clin. Res. Unit Blood Coagulation Thromb., Justus-Liebig-Univ., Giessen, D-6300, Fed. Rep. Ger.
SOURCE: J. Biol. Chem. (1987), 262(25), 12247-53
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interference of the heparin-neutralizing plasma component S protein (vitronectin) (mol. wt. (Mr) = 78,000) with heparin-catalyzed inhibition of coagulation factor Xa by antithrombin III (ATIII) was investigated in human plasma and in a purified system. In plasma, S protein effectively counteracted the anticoagulant activity of heparin, since factor Xa inhibition was markedly reduced in comparison to heparinized plasma deficient in S protein. By using purified components in the presence of heparin, S protein induced a concn.-dependent redn. of the inhibition rate of factor Xa by ATIII. This resulted in a decrease of the apparent pseudo-1st order rate const. by >10-fold at a physiol. ratio of ATIII to S protein. S protein not only counteracted the anticoagulant activity of com. heparin but also of low-Mr forms of heparin (mean Mr of 4500). The heparin-neutralizing activity of S protein was mainly expressed in the range 0.2-10 .mu.g/mL of high-Mr as well as low-Mr heparin. S protein and high-affinity heparin reacted with apparent 1:1 stoichiometry to form a complex with a dissocn. const. KD = 1 x 10-8M as detd. by a functional assay. As deduced from dot-blot anal., direct interaction of radiolabeled heparin with S protein revealed a KD = 4 x 10-8M. Heparin binding as well as heparin neutralization by S protein increased significantly when reduced/carboxymethylated or **guanidine**-treated S protein was employed, indicating the existence of a partly buried heparin-binding domain in native S protein. Radiolabeled heparin bound to the native protein mol. as well as to a BrCN fragment (Mr = 12,000) contg. the heparin-binding domain as demonstrated by direct binding on nitrocellulose replicas of SDS-polyacrylamide gels. Kinetic anal. revealed that the heparin neutralization activity of S protein in the inhibition of factor Xa by ATIII could be mimicked by a synthetic tridecapeptide from the N-terminal portion of the heparin-binding domain. Hence, the heparin-binding domain of S protein appears to be unique in binding to heparin and thereby neutralizing its anticoagulant activity in the inhibition of coagulation factors by ATIII. The induction of heparin binding and neutralization may be considered a possible physiol. mechanism initiated by conformational alteration of the S protein mol. Consequently, a secondary structure model of S protein is proposed in which the .beta.-pleated sheet structure of the heparin-binding domain is localized in a buried position within the protein mol.

IT **9005-49-6**, Heparin, biological studies
RL: **RCT (Reactant)**
(vitronectin binding and neutralization of, in blood-coagulation factor Xa inhibition by antithrombin III)
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d ibib abs hitstr 1

L107 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:219836 HCAPLUS
DOCUMENT NUMBER: 128:286337
TITLE: Processes for the preparation of low-affinity, low molecular weight heparins useful as antithrombotics
INVENTOR(S): Hirsh, Jack; Shaklee, Patrick N.; Knobloch, James E.; Weitz, Jeffrey I.; Young, Edward
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.; Shaklee, Patrick N.; Knobloch, James E.; Weitz, Jeffrey I.; Young, Edward
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814481	A1	19980409	WO 1997-US17849	19971001
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5767269	A	19980616	US 1996-722408	19961001
AU 9747441	A1	19980424	AU 1997-47441	19971001

PRIORITY APPLN. INFO.: US 1996-722408 19961001
WO 1997-US17849 19971001

AB The present invention generally relates to processes for prepg. low affinity, low mol. wt. heparins (LA-LWM-heparins) which are endowed with pharmacol. and therapeutic properties that are surprisingly advantageous. In one embodiment, the process comprises: (1) nitrous acid depolymn. of unfractionated **heparin** to yield low mol. wt. **heparin** (**LMWH**); (2) oxidn. of the resulting **LMWH** to open the ring structures the **nonsulfated uronic** acid moieties using, for example, **sodium** periodate; and (3) redn. of the oxidized **LMWH** to reduce the aldehydes (to alcs.) formed during the depolymn. and oxidn. steps using, for example, **sodium** borohydride. The resulting LA-LMW-heparins are capable of inactivating thrombin bound to fibrin within a thrombus or clot, whereby the ability of clot-bound thrombin to catalytically promote further clot accretion is substantially diminished or eliminated. As such, the resulting LA-LMW-heparins are useful for preventing thrombosis in the circuit of cardiac bypass app. and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, such as unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.

=> d ibib abs hitstr 2

L107 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:614342 HCAPLUS
DOCUMENT NUMBER: 125:265104
TITLE: Interaction between the **sulfated** lactobionic acid (LW 10082) and other antithrombotic agents in animal thrombosis model
AUTHOR(S): Giedrojc, Jan; Krupinski, Kazimierz; Breddin, Hans Klaus; Bielawiec, Michal
CORPORATE SOURCE: Department Haematology, Medical Academy, Bialystok, 15-276, Pol.
SOURCE: Pol. J. Pharmacol. (1996), 48(3), 317-322
CODEN: PJPAE3; ISSN: 1230-6002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the comparative antithrombotic properties of LW 10082, acetylsalicylic acid (Aspisol), low mol. wt. **heparin** (**LMWH**, CY 216) and **sodium heparin** using laser-induced thrombosis model. The animal model which has been used is well suited to observe platelet reactions to damaged endothelial cells and also to evaluate the effect of drugs on the formation of platelet thrombi. The rat mesenteric venules with a diam. of 20-30 .mu.m were injured by well defined argon laser lesion. The no. of laser injuries which were needed to induce a thrombus intermittently occluded the vessel was counted to quantitate the results. LW 10082 was injected s.c. 2 h prior to testing. The minimal ED of LW 10082 which significantly inhibited thrombus formation was 5 mg/kg. The antithrombotic effect of Aspisol has been investigated after its oral application at doses of 1, 5 and 10 mg/kg 2 h before studying the antithrombotic effect. The minimal ED for Aspisol was 10 mg/kg. The **LMWH** has been injected into the rat tail vein in doses of 1, 0.2 and 0.1 mg/kg 30 min before testing, 0.1 mg/kg did not have any antithrombotic effect. The minimal ED of the **sodium heparin** which significantly inhibited thrombus formation was 20 U/kg measured 30 min after its i.v. injection. The combination of minimal ED of LW 10082 and **LMWH** had a significant additive effect. There was a slight but not significant additive effect between LW 10082, Aspisol and **heparin sodium**. Our results suggest that combinations of LW10082 with **LMWH** may provide a new approach to more effective prophylaxis and treatment of venous or arterial thrombosis.

=> d ibib abs hitstr 3

L107 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:455068 HCAPLUS
DOCUMENT NUMBER: 122:209022
TITLE: Fluorescence and circular dichroism studies during the interactions of **sulfated** polysaccharides with antithrombin III
AUTHOR(S): Tanyi, A.; Benjamin, V.; Sadberry, A. J.; Doctor, V. M.
CORPORATE SOURCE: Dep. Chemistry, Prairie View A and M University, Prairie View, TX, 77446, USA
SOURCE: Thromb. Res. (1995), 77(6), 505-13
CODEN: THBRAA; ISSN: 0049-3848
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The changes in relative fluorescence of antithrombin III (AT-III) during its interaction with **sulfated** xylans were compared with that of **sulfated** glycosaminoglycans by measuring the ratio of the increase in fluorescence of AT-III in the presence of **sulfated** polysaccharide to the fluorescence of AT-III alone for various mass ratios. Interactions of corn cob xylan **sulfate** (CCXS) and **sodium** pentosan **polysulfate** (SP-54) with AT-III resulted in enhancements of relative fluorescence which were lower than com. **heparin**. At mass ratios below 1, heparan **sulfate** and low mol. wt. heparin (**LMWH**) gave increases in the relative fluorescence higher than that of com. heparin, while highly **sulfated** semisynthetic chondroitin **sulfates** A and C gave much smaller increases. The relative fluorescence enhancements of AT-III by heparan **sulfate**, com. heparin, **LMWH** and heparin derived pentasaccharide (HDP) increased with increasing mass ratios while the enhancements by CCXS, SP-54 and the highly **sulfated** chondroitin **sulfates** A and C were reversed at higher mass ratios. The estd. dissocn. consts. (kd) for the interaction of AT-III and the heparin-related compds. showed that heparan **sulfate** and **LMWH** gave the lowest kd values indicating a higher affinity for AT-III while com. heparin and HDP gave higher kd values, indicating a lower affinity for AT-III. SP-54 gave a kd value lower than CCXS, indicating a greater affinity for AT-III. A comparison of the near UV CD spectrum of AT-III alone and during its interaction with oat spelts xylan **sulfate** showed enhancements of the 2 arom. amino acid regions corresponding to phenylalanine and tryptophan.